Performance of pit and fissure sealants according to tooth characteristics: A systematic review and meta-analysis

Papageorgiou, Spyridon N ; Dimitraki, Dionysia ; Kotsanos, Nikolaos ; Bekes, Katrin ; van Waes, Hubertus

Abstract: OBJECTIVE: Aim of this systematic review was to assess the clinical performance of sealants on various teeth in an evidence-based manner. SOURCES: Five databases were searched from inception to February 2017. DATA: Randomized clinical studies on humans. METHODS: After duplicate study selection, data extraction, and risk of bias assessment according to the Cochrane guidelines, Paule-Mandel random-effects meta-analyses of Relative Risks (RRs) and their 95% confidence intervals (CIs) were calculated. RESULTS: A total of 16 randomized clinical trials with 2778 patients (male/female 49.1%/50.9%) and an average age of 8.4 years were included. No significant difference in either caries incidence of sealed teeth or sealant retention could be found according to (i) mouth side (right versus left), (ii) jaw (upper versus lower), (iii) and tooth type (1st permanent molar versus 2nd permanent molar/1st permanent molar versus 2nd deciduous molar/1st deciduous molar versus 2nd deciduous molar), based on evidence of very low to low quality. On the other side, compared to 1st permanent molars, sealed premolars were significantly less likely to develop caries (3 trials; RR=0.12; 95% CI=0.03 to 0.44; P=0.001) and less likely to experience loss of the sealant (5 trials; RR=0.33; 95% CI=0.20 to 0.54; P=0.001), both based on low to moderate quality evidence. CONCLUSIONS: The performance of pit and fissure sealants does not seem to be negatively affected by mouth side, jaw, and tooth type, apart from the exception of a favorable retention on premolars. CLINICAL SIGNIFICANCE: Based on existing evidence, pit and fissure sealants can be effectively applied on any deciduous or permanent posterior teeth without adverse effects on their clinical performance.

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TITLE PAGE

Performance of pit and fissure sealants according to tooth characteristics: a systematic review and meta-analysis

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A B S T R A C T

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Clinical Significance: Based on existing evidence, pit and fissure sealants can be effectively applied on any deciduous or permanent posterior teeth without adverse effects on their clinical performance.

BLINDED MANUSCRIPT

1. Introduction

1.1. Background

Dental caries remains the most common chronic disease amongst all oral conditions [1] with prevalence of untreated caries or caries experience ranging between 21% (children 6 - 11 years old), 58% (adolescents 12 - 19 years old), and 91% (adults older than 20 years old) [2,3], and differences according to geographic region [4] and family income [5].

Dental caries manifests itself as a continuous range of disease with increasing severity and tooth destruction, varying from subclinical changes to lesions with dentinal involvement [7,8]. Although the initial caries stages lack clear symptoms, this is not the case when lesions progress into dentine [9]. Dental caries can result in aesthetic, functional, or psychosocial complaints in a child's daily routine that ultimately affect their quality of life, including chewing and speech impairment, school absenteeism, decline in school performance, trouble sleeping, irritability, and refraining from smiling or speaking [10-13], while it is the primary cause of oral pain and tooth loss [9].

Overall, about half of all carious lesions are found in the pits and fissures of permanent posterior teeth [6], although caries is not confined solely to permanent teeth. This has to do with the direct influence of internal morphology of the interlobal groove-fossa system and caries progression [14], due to the easier bacterial accumulation, qualitative differences of pit-and-fissure plaque with smooth-surface plaque, and difficulty of plaque removal from the occlusal surfaces [8,15]. Additionally, fluoride is less effective at preventing caries in these secluded tooth surfaces than at smooth surfaces [16], due to the anatomical particularities of the former.

The procedure of 'sealing' the pits and fissures of teeth was introduced in the 1960s to protect the tooth from caries and includes the placement of a liquid material onto the occlusal surface (i.e. pits and fissures) of posterior teeth, thereby forming a layer that is bonded micromechanically and acts mainly as a barrier against acids and the subsequent mineral loss from within the tooth [17]. Pit-and-fissure sealants can be placed on either caries-free posterior teeth to prevent pit-and-fissure caries or on teeth with incipient caries lesions to prevent their progression to definitive caries [17]. There is a vast wealth of available clinical evidence about the effects of dental sealants. Recent systematic reviews and meta-analyses of randomized clinical trials concluded that pit and fissure sealants are effective and safe to prevent or arrest the progression of non-cavitated carious lesions compared with a control without sealants [19,20] and have a caries-preventive effect equal [21] or better [20,22] than fluoride varnishes. Additionally, the use of adhesive systems beneath pit-and-fissure sealants has been reported to increase the sealant's retention, with conventional etch-and-rinse systems being preferable to self-etching systems [18]. Finally, further uses of dental sealants include sealing palatal surfaces of anterior teeth to protect against erosive tooth wear [23], sealing anomalous dental morphologies like talon cusps or hypomineralizations [24,25], or sealing smooth enamel surfaces to protect against caries during orthodontic treatment [26], but these fall out of the scope of the present review.

1.2. Rationale

Although the overall efficacy of dental sealants has long been documented in randomized clinical trials and systematic reviews thereof [19,20,22], it remains unclear whether the clinical performance of sealants is affected by the various tooth types. The most recent evidence-based clinical practice guideline for the use of pit-and-fissure sealants published by the American Dental Association and the American Academy of Pediatric Dentistry in 2016 [27] recommended the use of sealants compared with nonuse in primary and permanent molars with both sound occlusal surfaces and non-cavitated occlusal carious lesions in children and adolescents. However, no distinction was made between 1st and 2nd molars, and premolars were not mentioned at all. Additionally, the guideline authors highlighted the need for additional studies assessing the effect of sealants in the primary dentition. This information could have direct implications on the clinical decision of which teeth should be sealed by the dentist. Therefore, the aim of the present systematic review was to answer the clinical question: "Is the clinical performance of dental sealants affected by tooth characteristics (like tooth type, jaw, or side, etc)"?

2. Materials and methods

2.1. Protocol and registration

The review's protocol was made a priori following the PRISMA-P statement [28], registered in PROSPERO (CRD42017058510), and all post hoc changes were appropriately noted. This systematic review was conducted and reported according to Cochrane Handbook [29] and PRISMA statement [30], respectively.

2.2. Eligibility criteria

According to the Participants-Intervention-Comparison-Outcome-Study design schema (PICOS), we included randomized clinical trials on human patients including at least one trial arm comparing the clinical performance of pit and fissure sealants with any other active, control, or placebo modality. We subsequently selected trials that compared any two or more different groups in terms of tooth characteristics (tooth type, jaw, or side). Excluded were non-clinical or non-randomized studies, case reports, animal studies, and studies that did not directly compare between different teeth.

2.3. Information sources and literature search

Five electronic databases were systematically searched by one author (SNP) without any limitations from inception up to February 23, 2017 (Appendix 1). Additionally, five sources (Google Scholar, International Standard Registered Clinical/soCial sTudy Number registry, Directory of Open Access Journals, Digital Dissertations, and metaRegister of Controlled Trials) and the reference/citation lists of included trials were manually searched for any additional trials. Authors of included trials were contacted for additional missed or ongoing trials. No limitations concerning publication language, publication year, or publication status were applied.

2.4. Study selection

The eligibility of identified studies was checked sequentially from their title, abstract, and full-text against the eligibility criteria by one author (SNP) and were subsequently checked independently by a second one (DD), with conflicts resolved by a third author (NK).

2.5. Data collection and data items

Study characteristics and numerical data were extracted from included trials independently by two authors (SNP, DD) using pre-defined and piloted extraction forms including: (i) study characteristics (design, clinical setting, country), (ii) patient characteristics (age, sex, status of sealed teeth), (iii) interventions used, (iv) follow-up, and (v) study outcome measures. The primary outcome of this systematic review was dental caries of the sealed tooth, while the secondary outcomes included combined (total or partial) loss of the sealant, total loss of the sealant, need for re-sealing, and replacement of the initial sealant by a restoration. Piloting of the forms was performed during the protocol stage until over 90% agreement was reached. Missing or unclear information was requested by the trials' authors and re-analyzed firsthand, when possible.

2.6. Risk of bias in individual trials

The risk of bias of included RCTs was assessed in duplicate by the same two authors (SNP, DD) using Cochrane's risk of bias tool [29]. A main risk of bias assessment was included in the systematic review pertaining to each trial's primary outcome.

2.7. Data synthesis

Meta-analysis was performed if similar interventions and control groups were compared and similar outcomes were measured. As the clinical performance of dental sealant might be affected by treatment-related characteristics (clinical setting, operator's experience, technique adequacy, materials used) or patient-related characteristics (age, sex, dietary or oral hygiene habits), a random-effects model was judged as clinically and statistically appropriate [31]. The novel random-effects model proposed by Paule and Mandel was preferred a priori over the more widely known DerSimonian and Laird method to estimate all pooled data, as it outperforms the latter [32]. Relative Risks (RR) and their corresponding 95% Confidence Intervals (CI) were calculated. Statistically significant results of binary meta-analyses were translated clinically using the Number Needed to Treat (NNT). If included trials had clustered data and raw data were acquired, we re-analyzed the trial's results ourselves with generalized linear regression accounting for clustering with robust standard errors. Comparisons among the various tooth categories were performed taking the 1st permanent molar as reference category, since this is the tooth most often being sealed, due to the predilection of dental caries for this tooth [33].

The extent and impact of between-study heterogeneity was assessed by inspecting the forest plots and calculating the tau^2 and the I^2, respectively; I^2 defines the proportion of total variability in the result explained by heterogeneity, and not chance [34]. The 95% CIs around tau^2 and I^2 were calculated [35] to quantify our uncertainty around these estimates. 95% predictive intervals were calculated for meta-analyses of ≥ 3 trials to incorporate existing heterogeneity and provide a range of possible effects for a future clinical setting [36]. All analyses were conducted in Stata SE version 14 (StataCorp LP, College Station, TX) by one author (SNP). A two side P-value ≤ 0.05 was considered significant for hypothesis-testing, except for P ≤ 0.10 used for tests of between-studies or between-subgroups heterogeneity [37].

2.8. Risk of bias across studies

The overall quality of clinical recommendations for each of the main outcomes was rated using the Grades of Recommendations, Assessment, Development, and Evaluation (GRADE) approach, as very low, low, moderate or high [38], using a novel format [39]. The minimal clinical important, large, and very large effects were defined as 1.5, 2.5, and 4.3 were adopted for the RR. The produced forest plots were augmented with contours denoting the magnitude of the observed effects [40].

2.9. Additional analyses and sensitivity analyses

Mixed-effects subgroup analyses were performed using pre-defined factors for meta-analyses with ≥ 5 studies. Reporting biases (including the possibility of publication bias) were assessed by drawing contour-enhanced funnel plots and testing for asymmetry with Egger's regression method [41] in meta-analyses of ≥ 10 studies [42]. Robustness of the meta-analyses was planned a priori to be checked with sensitivity analyses based on (i) exclusion of trials with high risk of bias, (ii) improvement of the GRADE classification, and (iii) exclusion of trials with reporting biases.

3. Results

3.1. Study selection

A total of 349 and 7 papers were identified through electronic and manual searches, respectively (Fig. 1). After removal of duplicates and initial screening by title or abstract, 100 papers were assessed using the eligibility criteria, and 20 papers were left as potentially eligible for this systematic review (Fig. 1; Appendix 2). In seven instances, trialists were contacted (Appendix 3), as additional data were needed to include their trials and in three cases raw or aggregate data were provided. Thus, a total of 16 papers, all pertaining to unique trials, were finally included in the systematic review (Appendix 2).

3.2. Study characteristics

The characteristics of the included randomized clinical trials can be seen in Table 1. Of these, 3 (19%) were parallel and 13 (81%) cluster randomized trials, conducted predominantly in universities (n=10; 63%) of 12 different countries. They included a total of 2778 patients (median 114 patients per trial; range 16 to 521) with male patients being the 49.1% (786 / 1600 patients among the 7 trials that reported patient sex), and with an average age of 8.4 years. Dental sealants were applied on caries-free teeth (n=8; 50%), on teeth with initial non-cavitated carious lesions (n=2; 13%), or a combination thereof (n=6; 38%). Various preparation protocols or sealant materials were tested in the included trials and reported either the review's primary outcome of caries (n=7; 44%) or the secondary outcome of retention (n=15; 94%).

3.3. Risk of bias within studies

The risk of bias for the included trials included is summarized in Fig. 2 and given in detail in Appendix 4. High risk of bias was found in 9 (56%) trials for at least one bias domain, with the most problematic being complete blinding of outcome assessments (missing in all 50% of the trials), randomization procedure (improper in 19% of the trials), and incomplete outcome data (in 6% of the trials).

3.4. Results of individual studies and data synthesis

The re-analysis of the two trials that graciously provided raw study data [43,44] can be seen in Appendix 5-7. The data synthesis of all reported outcomes at all time points from all identified trials are given in full in Appendix 8, but are not overly discussed. Focus in this review is given mainly at the review's two pre-defined outcomes: the primary outcome of caries incidence and the secondary outcome of sealant retention. For the analyses included in the main part of the review, only the longest follow-up is used from each included trial.

As far the caries incidence of sealed teeth is concerned, no significant differences could be found between teeth on the right or left side of the mouth and between maxillary and mandibular teeth (Table 2). Nevertheless, compared to sealed first permanent molars, sealed premolars were significantly less likely to develop caries (3 trials; RR = 0.07; 95% CI = 0.01 to 0.61; P = 0.013). However, since heterogeneity of the initial meta-analysis was very high (I^2 = 82%; 95% CI = 66% to 99%) a shorter follow-up was chosen for one of the meta-analyzed trials [45] (5 year instead of 15 year follow up) in order to make the three trials more compatible. Subsequently, sealed premolars were significantly less likely to develop caries than sealed molars (3 trials; RR = 0.12; 95% CI = 0.03 to 0.44; P = 0.001) with moderate heterogeneity (Fig. 3). This was translated to an NNT = 8.6 (rounded up to 9), which meant that an extra carious lesion would be avoided for every 9th premolar sealed. Finally, no significant difference in the caries incidence was found between sealed first and second permanent molars or between first and second deciduous molars.

As far as sealant retention is concerned, this was assessed as combined loss, by grouping total and partial loss of the sealant together (Table 3). No statistically significant difference in combined loss of the sealant could be found according to mouth side (right versus left side), jaw (upper versus lower), and tooth type (permanent 1st molar versus permanent 2nd molar/ permanent 1st molar versus deciduous 2nd molar/ deciduous 1st molar versus deciduous 2nd molar), with high heterogeneity in most cases, which was interpreted as statistical 'noise' (Fig. 3). The only significant difference in sealant retention found pertained to tooth type, where sealants on 1st or 2nd premolars were significantly less likely to be lost compared to sealants placed on 1st permanent molars (7 studies; RR = 0.42; 95% CI = 0.21 to 0.83; P = 0.013). However, since heterogeneity of the initial meta-analysis was very high (I^2 = 96%; 95% CI = 91% to 99%), one trial [45] was omitted and two arms pertaining to the same sealant material from the same trial [46] were pooled in order to reduce heterogeneity. Subsequently, sealants on premolars were significantly less likely to be lost than sealed 1st permanent molars (5 trials; RR = 0.33; 95% CI = 0.20 to 0.54; P = 0.001). Residual heterogeneity still remained high, but it affected only the magnitude and not the direction of effects (i.e. all trials were on the same side of the forest plot) and high uncertainty around the heterogeneity estimates was seen (I^2 = 81%; 95% CI = 0% to 96%). We therefore decided that heterogeneity posed no threat to the validity of meta-analyses results, which were translated to an NNT = 5.5 (rounded up to 6), which meant that an additional sealant loss would be avoided for every 6th premolar sealed.

3.5. Additional analyses

Subgroup analyses could be performed only for a handful of meta-analyses that included at least 5 trials (Appendix 9). Apart from minor differences according to the trial's follow-up, significant subgroup effects were seen according to the sealant material, where resin sealants with fluoride used on deciduous molars were more likely to be lost compared to 1st permanent molars, which was the opposite of what was seen for resin sealants without fluoride ($P < 0.10$). Additionally, sealed lower teeth were more likely to develop caries than upper sealed teeth, when either a fluoride resin sealant or a glass ionomer cement sealant was used than a resin sealant ($P < 0.10$). As however only a limited number of trials contributed to the analysis and no concrete conclusions could be drawn, caution is warranted until further research confirms or rejects these.

Reporting biases could be assessed only for one meta-analysis that included at least 10 trials (Table 2-3): the comparison of the secondary outcome (sealant loss) between maxillary and mandibular teeth. As such, both the contour-enhanced funnel plot (Fig. 4) and Egger's test (coefficient = -0.54; 95% CI = -1.89 to 0.81; P = 0.400) indicated no significant signs of bias.

3.6. Risk of bias across studies

Assessment of existing meta-evidence with the GRADE approach (Table 4-5) indicated that very low to low quality evidence supported all assessed comparisons, with the main limitation being inconsistency among trials (heterogeneity) and the fact that essentially observational data were extracted from the included randomized trials. For the statistically significant differences between sealant placed on premolars or 1st permanent molars (both for caries and sealant loss) low to moderate quality of meta-evidence was found, with the main limitation being the different baseline caries risk of untreated premolars and molars.

3.7. Sensitivity analyses

Sensitivity analyses could not be performed for any of the meta-analyses, as the main reason for downgrading the quality of evidence was inconsistency (heterogeneity). However, this was due to a general scattering of trials on both sides of the forest plot, characteristic of the absence of a specific treatment relationship, and omission of single trials could not produce a homogenous group of trials. The two instances of statistically significant meta-analyses were on the other side supported by high quality evidence and therefore no sensitivity analysis was needed.

4. Discussion

4.1. Summary of evidence

The present systematic review evaluated the clinical performance of pit and fissure sealants placed on the occlusal surfaces of caries-free or non-cavitated carious posterior teeth to prevent caries and its progression. According to existing evidence from 16 identified randomized clinical trials including 2778 patients tooth-related characteristics had little to no influence on the clinical performance of pit and fissure sealants.

According to the results of the meta-analyses, no significant difference between sealants placed on upper and lower teeth could be seen in terms of either dental caries or retention of the sealant ($P > 0.05$ for both; Tables 2-3). Potential differences in the bonding performance of dental materials (including pit and fissure sealants) between maxillary and mandibular teeth have been attributed to the greater sensitivity to saliva contamination of the latter. This is reflected in the superior retention of fissure sealants on maxillary molars than on the occlusal surface of mandibular molars found by some studies [47,48], although these were not consistent [49]. Another proposed hypothesis for differences between upper and lower teeth pertains to the markedly longer grooves of permanent mandibular molars, which might limit the retention of the sealant [50]. However, reported differences between maxillary and mandibular teeth in the literature are not consistent [51-53] and no clear relationship can be established.

As far as differences between different permanent posterior teeth are concerned, similar clinical performance of sealants, placed on 1st and 2nd permanent molars, was seen. The occlusal surface of second primary molars is larger than first primary molars, enabling convenience in the placement and visual assessment of sealants because of broader occlusal surface. However, the caries susceptibility of 2nd permanent molars is similar to that of the 1st permanent molars and therefore, the benefit from sealing should not be underestimated.

On the other side, sealants placed on premolars had significantly less caries of the sealed tooth (NNT of 9) and significantly better retention (NNT of 6) than 1st permanent molars. This is in agreement with previous studies that report higher sealant retention rates than of premolars compared to 1st molars [53-56] and has been attributed by Handelman *et al.* [53] not to inherent difference in the anatomy of these teeth, but rather the much larger total area of the pit and fissure system. In this sense, Jensen *et al.* [55] reported that the amount of sealant material placed on the molar teeth is twice as much as the amount placed on premolars, and therefore is exposed to overall twice the risk of failure within the material. Other explanations for this include easier access to the premolar's surface [45], easier isolation [56], variations in the morphology and microscopic structure of the enamel in the different tooth types [45], and exposure to lower occlusal loading than molars [56]. However, it is important here to stress out that the observed difference in the caries incidence of sealed teeth does not lie solely with the significant better retention of premolar sealant, but also to the inherent lower overall caries incidence of premolars compared to molars, even when left untreated [33,57]. The caries susceptibility of premolars should not be overall underestimated, since they are the second most prone to caries permanent tooth after permanent molars [57]. However, they are significantly less prone to pit and fissure caries than molars [57], which might confound the comparative effectiveness of sealants in safeguarding against pit and fissure caries, and no robust conclusions can be drawn regarding this outcome.

Results of the present meta-analysis seem to support the recent guideline of the American Dental Association suggesting the sealing of both primary and permanent molars [27], as no significant difference in sealant performance between primary and permanent molars was seen (Tables 2-3). Potential differences in the retention of sealants placed in deciduous or permanent teeth have been attributed to the shallower pit and fissures of the former [58], which might support the use of low-viscosity composite resins over conventional ones to enhance the penetration of the sealant [59]. Likewise, dental sealants seemed to work similarly good on 1st or 2nd deciduous molars in terms of caries prevention and sealant retention, although only one trial contributed to this analysis (Tables 2-3).

The concept of risk-based sealant application [60] can form the basis of the rationale for and efficacy of sealant placement and specific considerations like tooth morphology, caries history, fluoride history, and oral hygiene can be assessed by an experienced clinician in terms of indication for sealant placement [14,61]. However, post-eruptive age alone should not be used as a major criterion for decision-making, as the caries risk on surfaces with pits and fissures might continue into adulthood and therefore, any tooth at any age could potentially benefit from sealants [61]. On the other side, casual recommendations on a universal level cannot be made for the various deciduous and permanent posterior teeth without taking into considerations other factors including cost-effectiveness [62,63] and potential side-effects in terms of bisphenol-a release [64] or estrogenicity [65]. Therefore, additional research is needed in terms of clinical efficacy, cost-effectiveness, and potential side effects based on well-conducted longitudinal trials that take into account differences in the clinical performance of pit and fissure sealants for different teeth and take clustering effects into consideration.

4.2. Strengths and limitations

The strengths of this systematic review consist in a priori registration in PROSPERO and the use of robust systematic review and meta-analysis procedures [32,36,38,40,66-69]. As no specific patient- or tooth-related eligibility criteria were adopted and a wide array of clinical settings in the private or public sector were included in the present systematic review, its conclusions could be generalized to the average patient.

However, some limitations are also present in this study. First and foremost, additional individual patient data couldn't be obtained in many instances through attempts to communicate with trialists (Appendix 3), which precluded re-analysis to take into account baseline confounding and clustering effects. This precluded the direct assessment of the influence of many factors important to the performance of dental sealants, including among others the patient's age, which can have a direct effect. Although multiple attempts were made to request patient raw data and re-analyzed clustering adjusted estimates incorporating confounding effects, these were met predominantly with failure and additional research is needed to clarify this. Moreover, the limited number of included trials means that meta-analyses of some outcomes might lack sufficient power and did not enable robust assessments of heterogeneity, subgroup analyses, small-study effects, and reporting biases for most of the outcomes. This limitation is exacerbated by the fact that many potentially eligible trials either did not report or reported incompletely if any comparisons between different teeth were made (Appendix 2) and therefore, might not have been identified or could not contribute to the analyses. Finally, although randomized trials were included in the present review, essentially observational data were extracted from them, as no randomization according to tooth characteristics could be performed.

5. Conclusions

Based on the results of this comprehensive systematic review of randomized clinical trials the performance of pit and fissure sealants in terms of caries of the sealed tooth or retention loss of the sealant do not seem to be negatively affected by mouth side, jaw, and tooth type. The only exception was the use of pit and fissure sealants on premolars, which was associated with lower sealant failure rate compared to the use of pit and fissure sealants on the first permanent molar, indicating favorable performance. From the perspective of the sealant's clinical performance all deciduous or permanent posterior teeth could be effectively sealed.

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Figure Legends

Fig. 1. PRISMA flow diagram for the identification and selection of studies eligible for this systematic review.

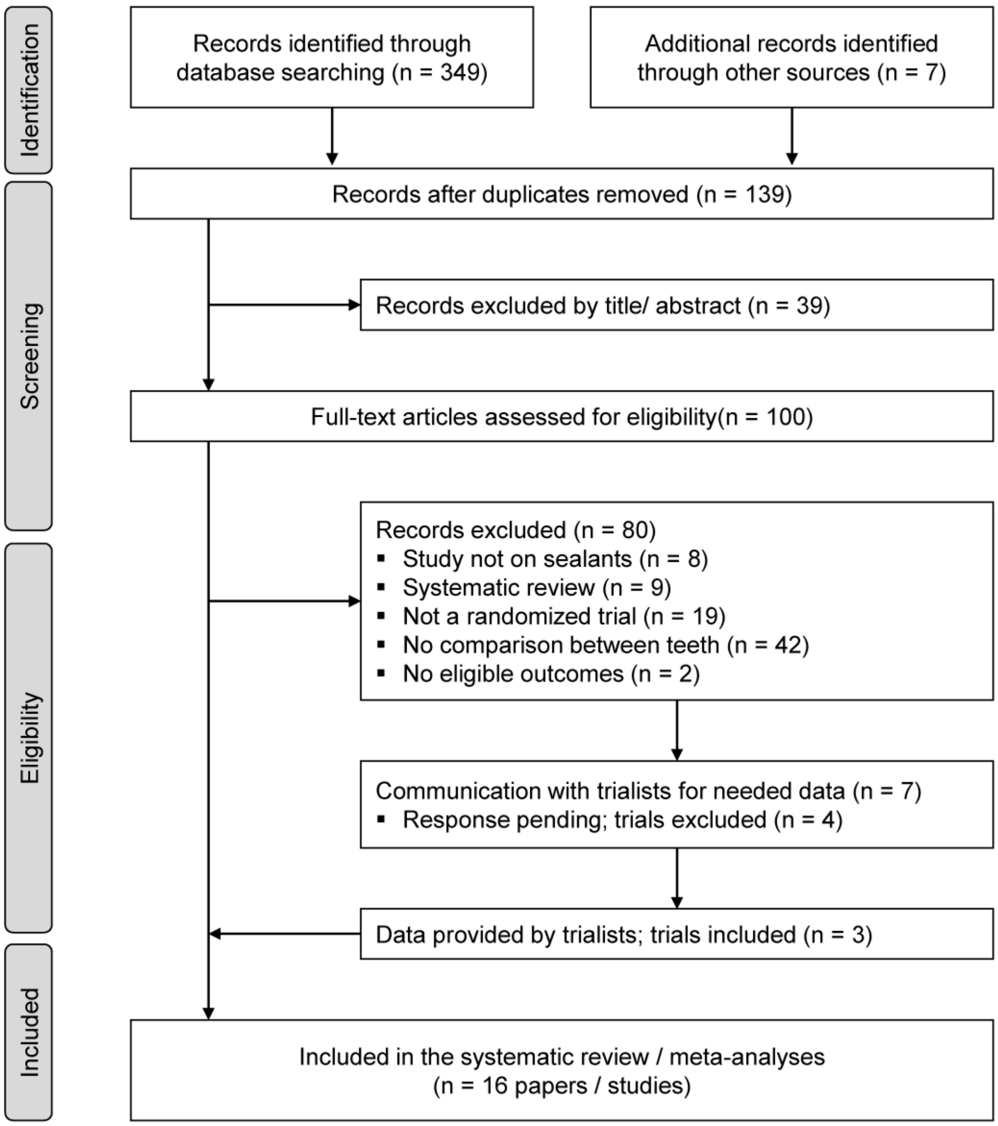

Fig. 2. Risk of bias summary of the included trials.

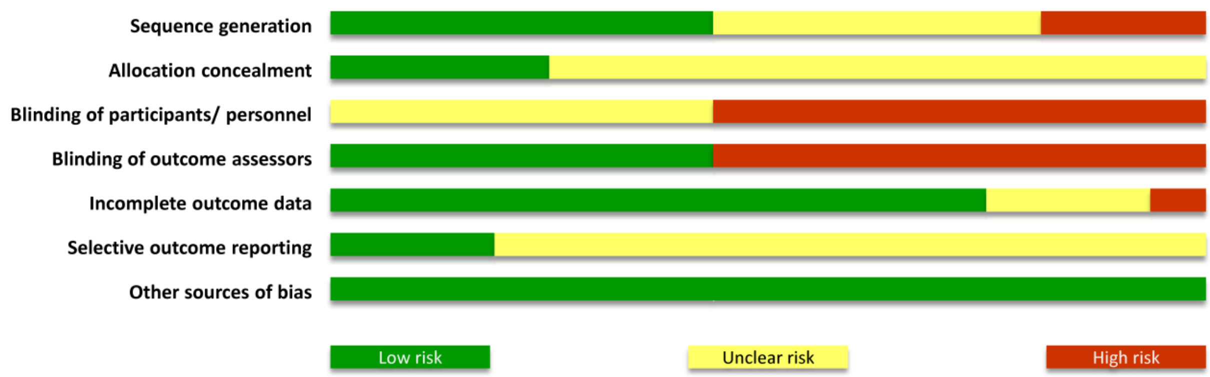

Fig. 3. Contour-enhanced cumulative forest plot presenting the results of random-effects meta-analyses for the primary and secondary outcome of this systematic review. The forest plot has been enhanced with grey contours starting from small effect magnitude (lighter gray in the middle) and moving outwards to areas of medium, large, and very large effect magnitude, based on relative risk cut-offs of 1.5, 2.5, and 4.3 (or 0.67, 0.4, 0.23).

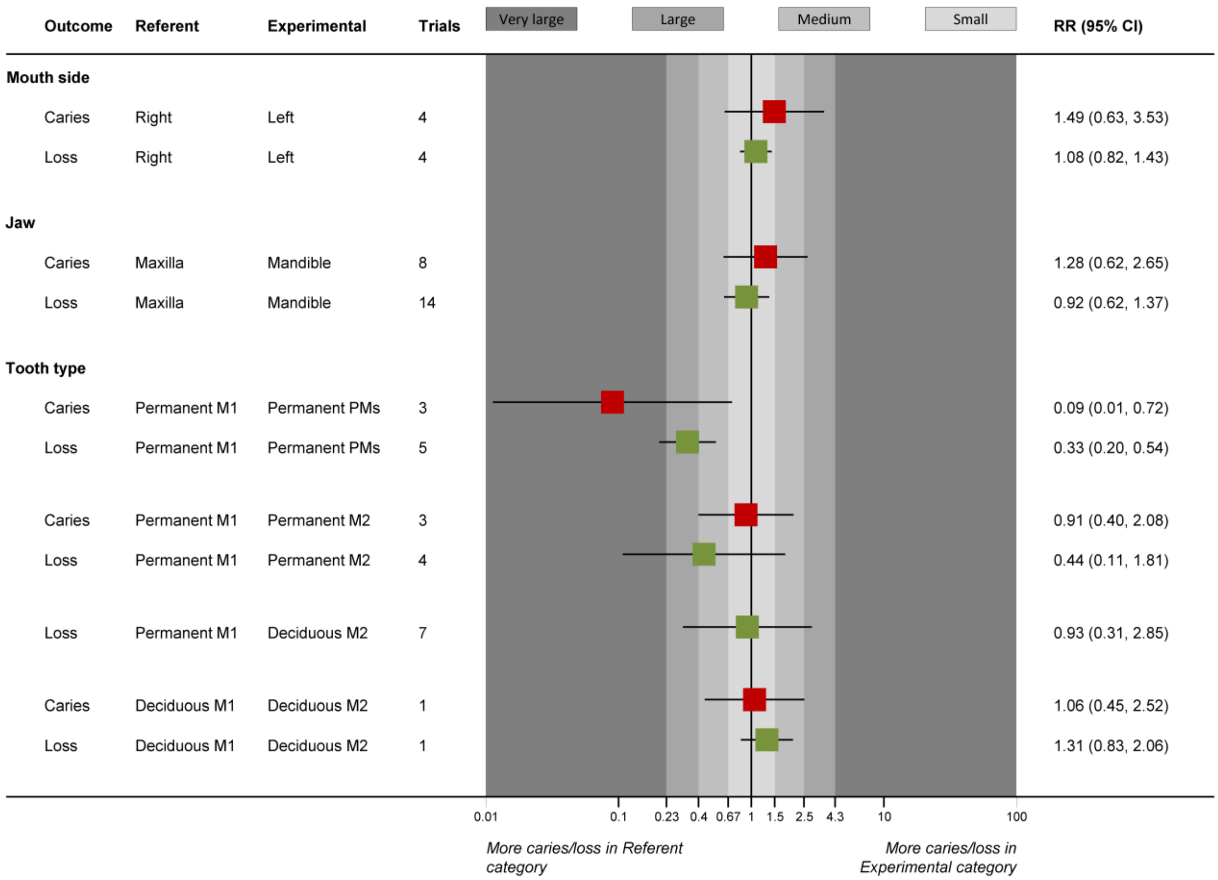

Fig. 4. Contour-enhanced funnel plot to assess the possibility and impact of reporting biases (including publication bias) for the comparison of the secondary outcome (sealant loss) between maxillary and mandibular teeth.

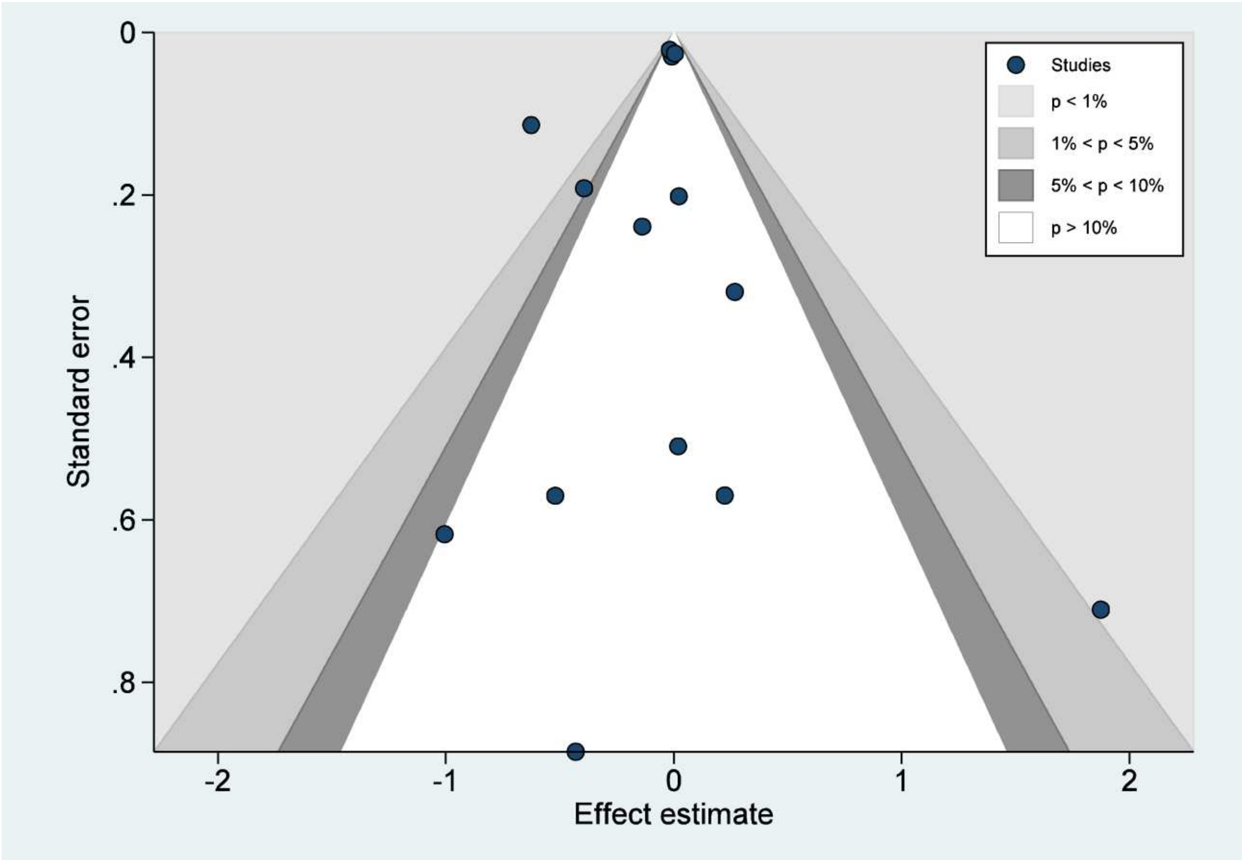

Table 1
Characteristics of included trials.

Nr	Study	Design; setting; country§	Patients (M/F); mean age	Caries*	Intervention	FU	Outcome
1	Baca 2007	smRCT; Uni; ESP	56 (NR); 7.3 yrs	No	Different materials; SL (Delton; Delton Plus; Concise; OptiBond Solo)	12	Retention (total)
2	Bhushan 2017	smRCT; Uni; IND	50 (NR); (6-8 yrs)	No	AE vs AE-air abrasion; SL (NR)	6	Retention (Simonsen)
3	Corona 2005	smRCT; Uni; BRA	40 (NR); (4-7 yrs)	No	Different materials; SL (Fluroshield; Bond 1+Flow it!)	12	Retention (Tonn & Ryge)
4	de Oliveira 2013	smRCT; Uni; BRA	80 (NR); (6-8 yrs)	Both	Different materials; SL (GC Fuji Triage) vs non-SL (F varnish)	18	Retention (Simonsen)
5	Erdemir 2014	smRCT; Uni; TUR	34 (18/16); (16-22 yrs)	Yes	Different materials; SL (Helioseal F; Tetric Evo Flow)	24	Retention (Tonn & Ryge); ICDAS II; caries
6	Grande 2000	smRCT; Uni; BRA	38 (15/23); 14 yrs	No	Different materials; SL (Delton; OptiBond)	30	Retention (Tonn & Ryge)
7	Handelman 1987	smRCT; Uni; GBR	159 (NR); 13.4 yrs	Both	Different materials; SL (Delton; Nuva-Cote)	24	Retention (total & partial)
8	Honkala 2015	smRCT; Uni; KWT	147 (76/71); 4.1 yrs	Both	Different materials; SL (Clinpro) vs non-SL (F varnish)	12	ICDAS; caries (dev/prog); retention (total & partial)
9	Jodkowska 2008	smRCT; schools; POL	360 (NR); (7-8 yrs)	No	Different materials (Concise Brand White; Concise Enamel Bond; Nuva-Seal)	180	Retention (total & partial); DMFT/DMFS; caries reduction; prevented fraction; net gain;
10	Karaman 2013	smRCT; Uni; TUR	16 (1/15); 21.0 yrs	No	AE vs Laser-etch; SL (Clinpro)	24	Retention (total & partial)
11	Li 1981	smRCT; clinic; USA	200 (NR); (5-16 yrs)	No	Different materials; SL (Delton; Nuva-Seal)	24	Retention; net gain; reseal need; caries (dev)
12	Liu 2012	pRCT; schools; CHN	501 (250/251); 9.1 yrs	Both	Different materials; SL (Clinpro) vs non-SL (F varnish/SDF) vs placebo	24	ICDAS; retention; dentin caries
13	Muller-Bolla 2013	smRCT; schools; FRA	343 (177/166); 6.4 yrs	Both	Efficacy; SL (Delton Plus) vs no treatment	12	Retention (total & partial); ICDAS
14	Poulsen 2001	smRCT; health center; SYR	179 (NR); 7 yrs	Both	Different materials; SL (Delton; Fuji III)	36	Retention (total & partial); caries
15	Qvist 2017	pRCT; clinics; DNK	521 (249/272); (6-17 yrs)	Yes	Different materials (SL vs non-SL)	84	Replacement need; caries progression
16	Sgavioli 2000	pRCT; Uni; BRA	60 (NR); (8-15 yrs)	No	Different materials; SL (Fluroshield) with or without topical F	12	Retention (total & partial)

AE, acid-etch-technique; DMFT/DMFS, decayed missing filled teeth/surfaces index; F, fluoride; FU, follow-up in months; ICDAS, International Caries Detection and Assessment System; M/F, male/female; NR, not reported; pRCT, parallel randomized clinical trial; SL, sealant; smRCT, split mouth randomized clinical trial; Uni, university clinic; yrs, years.
§ Countries are reported according to their ISO alpha-3 codes.
*Sealed tooth caries lesions pertained to initial carious non-cavitated lesions.

Table 2

Random-effects meta-analyses on the primary outcome of this review (caries incidence of the sealed tooth).

Referent	Experimental	Trials	RR (95% CI)	P	tau^2 (95% CI)	I^2 (95% CI)	95% prediction
Right	Left	4	1.49 (0.62,3.55)	0.372	0.56 (0,5.46)	74 (0,96)	0.04,63.43
Maxilla	Mandible	8	1.28 (0.62,2.62)	0.503	0.74 (0,2.26)	80 (0,92)	0.13,12.56
Permanent M1	Permanent PMs	3*	0.09 (0.01,0.72)	0.023	2.43 (0,50.00)	75 (0,99)	0.00,>1000
Permanent M1	Permanent M2	3	0.91 (0.40,2.06)	0.817	0.44 (0,14.69)	86 (0,100)	0.00,>1000
Deciduous M1	Deciduous M2	1	1.06 (0.45,2.49)	0.899	na	na	na

RR, relative risk; CI, confidence interval; PM, premolar; M, molar; na, not applicable.
*Initial met-analysis (3 trials; RR [95% CI]=0.07 [0.01,0.61]; P=0.015; tau^2 [95% CI]= 2.79 [1.18,50.00]; I^2 [95% CI]=82% [66%,99%]; 95% prediction=0,>1000) modified by including a shorter follow-up for one trial (5 years instead of 15 years) to make it more homogenous.

Table 3

Random-effects meta-analyses on the secondary outcome of this review (total or partial loss of the sealant).

Referent	Experimental	Studies	RR (95% CI)	P	tau^2 (95% CI)	I^2 (95% CI)	95% prediction
Right	Left	4	1.08 (0.82,1.43)	0.576	0.06 (0,0.84)	97 (0,100)	0.31,3.75
Maxilla	Mandible	14	0.92 (0.62,1.37)	0.692	0.44 (0.25,1.11)	99 (99,100)	0.20,4.16
Permanent M1	Permanent PMs*,**	5	0.33 (0.20,0.54)	<0.001	0.23 (0,1.40)	81 (0,96)	0.06,1.85
Permanent M1	Permanent M2	4	0.44 (0.11,1.80)	0.255	1.64 (0,19.74)	95 (0,100)	0.00,244.40
Permanent M1	Deciduous M2	7	0.93 (0.31,2.83)	0.900	1.74 (0.91,7.38)	89 (82,97)	0.02,36.82
Deciduous M1	Deciduous M2	1	1.31 (0.83,2.06)	0.249	na	na	na

RR, relative risk; CI, confidence interval; PM, premolar; M, molar; na, not applicable.

*Separate meta-analyses of first permanent molars versus first premolars (2 trials) or first permanent molars versus second premolars (2 trials) omitted and incorporated into overall meta-analysis of first permanent molars versus first/second premolars (7 trials)

** Initial meta-analysis: (7 trials; RR [95% CI]=0.42 [0.21,0.83]; P=0.013; tau^2 [95% CI]= 0.69 [0.32,3.51]; I^2 [95% CI]=96% [91%,99%]; 95% prediction=0.04,4.25); one trial omitted (Jodkowska 2005) and two trial arms (Karaman 2013) pertaining to the same material combined to reduce heterogeneity.

Table 4

GRADE Summary of Findings Table for the primary outcome (caries of sealed teeth).

		Anticipated absolute effects[*] (95% CI)				
Outcome **Studies (teeth)**	**RR** **(95% CI)**	**Referent[*]**	**Experimental**	**Difference**	**Quality of the evidence (GRADE)[a]**	**What happens**
Caries by mouth side 4 trials (1044 teeth)	1.49 (0.62,3.55)	***Right side*** 7.0%	***Left side*** 10.4% (4.3% to 24.9%)	3.4% more caries (2.7% less to 17.9% more)	⊕⊕○○ low	There may be little or no difference
Caries by jaw 8 trials (2136 teeth)	1.28 (0.62, 2.62)	***Upper jaw*** 7.0%	***Lower jaw*** 9.0% (4.3% to 18.3%)	2.0% more caries (2.7% less to 11.3% more)	⊕○○○ very low[b] due to inconsistency	There may be little or no difference
Caries by tooth type 3 trials (1395 teeth)	0.09 (0.01,0.72)	***$_{perm}$M1*** 13.2%	***$_{perm}$PMs*** 1.2% (0.1% to 9.5%)	12.0% less caries (3.7% to 13.1% less)	⊕⊕○○ low [c] due to effect magnitude	There might be less caries under sealed premolars
Caries by tooth type 3 trials (1117 teeth)	0.91 (0.40,2.06)	***$_{perm}$M1*** 18.7%	***$_{perm}$M2*** 17.0% (7.5% to 38.5%)	0.3% less caries (11.2% less to 19.8% more)	⊕○○○ very low[b] due to inconsistency	There may be little or no difference
Caries by tooth type 1 trial (265 teeth)	1.06 (0.45,2.49)	***$_{decid}$M1*** 6.6%	***$_{decid}$M2*** 7.0% (3.0% to 16.4%)	0.4% more caries (3.6% less to 9.8% more)	⊕○○○ very low[b] due to inconsistency	There may be little or no difference

Abbreviations: CI, Confidence interval; RR, relative risk; GRADE, Grading of Recommendations Assessment, Development and Evaluation.
Clinical performance of pit and fissure sealants placed on various teeth.
Patient or population: patients receiving pit and fissure sealants for caries prevention.
Settings: universities, schools, health centers, and clinics (Brazil, China, Dennmark, France, Great Britain, India, Kuwait, Poland, Spain, Syria, Turkey, USA).
[*] Reponse or risk in the control group is based on the average of included studies.
[a] Although randomized trials were included, essentially observational data is used from them. They are therefore treated as non-randomized trials in terms of quality of evidence, which starts from low.
[b] Downgraded by one due to high heterogeneity, which remained unexplained.
[c] GRADE for this could have been upgraded, since a very large effect magnitude was seen. As however, untreated premolars and molars have different caries prevalence, which could have confounded the results, GRADE was not upgraded.

Table 5

GRADE Summary of Findings Table for the secondary outcome (combined loss of the sealant).

		Anticipated absolute effects* (95% CI)				
Outcome Studies (teeth)	**RR (95% CI)**	**Referent***	**Experimental**	**Difference**	**Quality of the evidence (GRADE)** [a]	**What happens**
Sealant loss by mouth side 4 trials (1029 teeth)	1.08 (0.82,1.43)	***Right side*** 57.9%	***Left side*** 62.5% (47.5% to 82.8%)	4.6% more loss (10.4% less to 24.9% more)	⊕○○○ very low[b] due to inconsistency	There may be little or no difference
Sealant loss by jaw 14 trials (2995 teeth)	0.92 (0.62,1.37)	***Upper*** 36.4%	***Lower*** 33.5% (22.6% to 49.9%)	2.9% less loss (13.8% less to 13.5% more)	⊕○○○ very low[b] due to inconsistency	There may be little or no difference
Sealant loss by tooth type 5 trials (2931 teeth)	0.33 (0.20,0.54)	***permM1*** 26.8%	***permPMs*** 8.6% (5.4% to 14.5%)	18.2 less loss (12.3% to 21.4% less)	⊕⊕⊕○ moderate[c] due to effect magnitude	Less sealants loss with premolars
Sealant loss by tooth type 4 trials (1117 teeth)	0.44 (0.11,1.80)	***permM1*** 31.1%	***permM2*** 13.7% (3.4% to 56.0%)	17.4% less loss (27.7% less to 24.9% more)	⊕○○○ very low[b] due to inconsistency	There may be little or no difference
Sealant loss by tooth type 7 trials (826 teeth)	0.93 (0.31,2.83)	***permM1*** 21.7%	***decidM2*** 20.2% (6.7% to 61.4%)	1.5% less loss (15.0% less to 39.7% more)	⊕○○○ very low[b] due to inconsistency	There may be little or no difference
Sealant loss by tooth type 1 trial (265 teeth)	1.31 (0.83,2.06)	***decidM1*** 19.3%	***decidM2*** 25.3% (16.0% to 39.8%)	6.0% more loss (3.3% less to 20.5% more)	⊕○○○ very low[b] due to inconsistency	There may be little or no difference

Abbreviations: CI, Confidence interval; RR, relative risk; GRADE, Grading of Recommendations Assessment, Development and Evaluation.
Clinical performance of pit and fissure sealants placed on various teeth.
Patient or population: patients receiving pit and fissure sealants for caries prevention.
Settings: universities, schools, health centers, and clinics (Brazil, China, Dennmark, France, Great Britain, India, Kuwait, Poland, Spain, Syria, Turkey, USA).
[*] Reponse or risk in the control group is based on the average of included studies.
[a] Although randomized trials were included, essentially observational data is used from them. They are therefore treated as non-randomized trials in terms of quality of evidence, which starts from low.
[b] Downgraded by one due to high heterogeneity, which remained unexplained.
[c] Upgraded for large effect magnitude; high heterogeneity still remained after modifications, but it affected only the effect magnitude and not direction and high uncertainty around the heterogeneity estimates was seen; we therefore decided that heterogeneity posed no threat to the results validity.

Performance of pit and fissure sealants according to tooth characteristics: a systematic review and meta-analysis

SUPPLEMENTARY MATERIAL

Appendix 1. Search strategies used for every database with the corresponding hits (last search February 23, 2017)

MEDLINE (via PubMed)			Scopus			WOK			CENTRAL			VHL		
Search strategy	Limits	Hits	Search strategy	Limits	Hits	Search strategy	Limits	Hits	Search strategy	Limits	Hits	Search strategy	Limits	Hits
sealant* AND ("second molar" OR "second molars")	RCTs; Humans	11	sealant* AND ("second molar" OR "second molars") AND random*	Dentistry; Humans	14	Same as Scopus	Dent istry	8	Same as Scopus		10	Same as Scopus		1
sealant* AND ("first molar" OR "first molars")		41	sealant* AND ("first molar" OR "first molars") AND random*		39	Same as Scopus		22	Same as Scopus		28	Same as Scopus		0
sealant* AND ("first premolar" OR "first premolars")		3	sealant* AND ("first premolar" OR "first premolars") AND random*		4	Same as Scopus		0	Same as Scopus		3	Same as Scopus		0
sealant* AND ("second premolar" OR "second premolars")		0	sealant* AND ("second premolar" OR "second premolars") AND random*		1	Same as Scopus		0	Same as Scopus		0	Same as Scopus		0
sealant* AND ("first primary molar" OR "first primary molars")		4	sealant* AND ("first primary molar" OR "first primary molars") AND random*		3	Same as Scopus		1	Same as Scopus		4	Same as Scopus		0
sealant* AND ("second primary molar" OR "second primary molars")		3	sealant* AND ("second primary molar" OR "second primary molars") AND random*		3	Same as Scopus		1	Same as Scopus		3	Same as Scopus		0
sealant* AND ("primary first molar" OR "primary first molars")		1	sealant* AND ("primary first molar" OR "primary first molars") AND random*		1	Same as Scopus		1	Same as Scopus		1	Same as Scopus		0
sealant* AND ("primary second molar" OR "primary second molars")		3	sealant* AND ("primary second molar" OR "primary second molars") AND random*		5	Same as Scopus		1	Same as Scopus		1	Same as Scopus		0
sealant* AND (tooth OR teeth OR molar*) AND (primary OR temporary* OR deciduous*) AND permanent		24	sealant* AND (tooth OR teeth OR molar*) AND (primary OR temporary* OR deciduous*) AND permanent AND random*		41	Same as Scopus		34	Same as Scopus		20	Same as Scopus		1
sealant* AND ("tooth type" OR "tooth category")		3	sealant* AND ("tooth type" OR "tooth category") AND random*		3	Same as Scopus		0	Same as Scopus		2	Same as Scopus		0
SUM		**93**	**SUM**		**114**	**SUM**		**68**	**SUM**		**72**	**SUM**		**2**

WOK, Web of Knowledge; VHL, Virtual Health Library; RCT, randomized clinical trial.

Appendix 2. List of all included/ excluded studies, with reasons.

Nr.	Paper	Status
	Excluded papers	
1	Agrawal A, Shigli A. Comparison of six different methods of cleaning and preparing occlusal fissure surface before placement of pit and fissure sealant: an in vitro study. Journal of the Indian Society of Pedodontics and Preventive Dentistry. 2012;30(1):51-5.	Excluded by title
2	Chadwick BL, Treasure ET. Primary care research: difficulties recruiting preschool children to clinical trials. International journal of paediatric dentistry. 2005;15(3):197-204.	Excluded by title
3	Clarkson JE, Turner S, Grimshaw JM, Ramsay CR, Johnston M, Scott A, et al. Changing clinicians' behavior: a randomized controlled trial of fees and education. J Dent Res 2008;87(7):640-4.	Excluded by title
4	Mattos-Silveira J, Floriano I, Ferreira FR, Vigano ME, Frizzo MA, Reyes A, et al. New proposal of silver diamine fluoride use in arresting approximal caries: study protocol for a randomized controlled trial. Trials. 2014;15:448.	Excluded by title
5	Raucci-Neto W, de Castro-Raucci LM, Lepri CP, Faraoni-Romano JJ, Gomes da Silva JM, Palma-Dibb RG. Nd:YAG laser in occlusal caries prevention of primary teeth: a randomized clinical trial. Lasers in medical science. 2015;30(2):761-8.	Excluded by title
6	Sajjan PG, Nagesh L, Sajjanar M, Reddy SK, Venktesh UG. Comparative evaluation of chlorhexidine varnish and fluoride varnish on plaque Streptococcus mutans count--an in vivo study. International journal of dental hygiene. 2013;11(3):191-7.	Excluded by title
7	Stephen KW, Kay EJ, Tullis JI. Combined fluoride therapies. A 6-year double-blind school-based preventive dentistry study in Inverness, Scotland. Community Dent Oral Epidemiol 1990;18(5):244-8.	Excluded by title
8	Yilmaz Y, Keles S, Mete A. Temperature changes in the pulpal chamber and the sealing performance of various methods of direct pulp capping of primary teeth. European journal of paediatric dentistry : official journal of European Academy of Paediatric Dentistry. 2013;14(2):95-100.	Excluded by title
9	Yoon RK, Chussid S. Topical anesthesia for rubber dam clamp placement in sealant placement: comparison of lidocaine/prilocaine gel and benzocaine. Pediatr Dent 2009;31(5):377-81.	Excluded by title
10	[No authors] Evidenced-Based Review of Clinical Studies on Direct Pulp Capping. Journal of Endodontics. 2009;35(8):1152-4.	Excluded by title
11	Ahrari F, Nojoomian M, Moosavi H. Clinical evaluation of bonded Amalgam restorations in endodontically treated premolar teeth: A one-year evaluation. Journal of Contemporary Dental Practice. 2010;11(5):9-16.	Excluded by title
12	Canoglu H, Tekcicek MU, Cehreli ZC. Comparison of conventional, rotary, and ultrasonic preparation, different final irrigation regimens, and 2 sealers in primary molar root canal therapy. Pediatr Dent 2006;28(6):518-23.	Excluded by title
13	Dilley DC, Vann Jr WF, Oldenburg TR, Crisp RM. Time required for placement of composite versus amalgam restorations. ASDC journal of dentistry for children. 1990;57(3):177-83.	Excluded by title
14	Ricketts DNJ, Pitts NB. Novel operative treatment options. Monographs in Oral Science2009. p. 174-87.	Excluded by title
15	Riordan PJ. Secular changes in treatment in a school dental service. Community dental health. 1995;12(4):221-5.	Excluded by title
16	Saemundsson SR, Slade GD, Spencer AJ, Davies MJ. The basis for clinicians' caries risk grouping in children. Pediatr Dent 1997;19(5):331-8.	Excluded by title
17	Stephen KW, Kay EJ, Tullis JI. Combined fluoride therapies. Community Dent Oral Epidemiol 1990;18(5):244-8.	Excluded by title
18	Sundberg H, Mejàre I, Espelid I, Tveit AB. Swedish dentists' decisions on preparation techniques and restorative materials. Acta odontologica Scandinavica. 2000;58(3):135-41.	Excluded by title
19	Frencken JE, van't Hof MA, Taifour D, Al-Zaher I. Effectiveness of ART and traditional amalgam approach in restoring single-surface cavities in posterior teeth of permanent dentitions in school children after 6.3 years. Community Dent Oral Epidemiol 2007;35(3):207-14.	Excluded by title
20	Khalefa M, Finke C, Jost-Brinkmann PG. Effects of air-polishing devices with different abrasives on bovine primary and second teeth and deciduous human teeth. Journal of Orofacial Orthopedics-Fortschritte Der Kieferorthopadie. 2013;74(5):370-80.	Excluded by title
21	Mandari GJ, Frencken JE, van't Hof MA. Six-year success rates of occlusal amalgam and glass-ionomer restorations placed using three minimal intervention approaches. Caries Res 2003;37(4):246-53.	Excluded by title
22	Mortensen D, Ekstrand KR, Twetman S. Detection of occlusal caries with impedance spectroscopy and laser fluorescence before and after placement of fissure sealants: An in vitro study. American journal of dentistry. 2016;29(4):229-33.	Excluded by title
23	Van de Hoef N, Van Amerongen E. Influence of local anaesthesia on the quality of class II glass ionomer restorations. International journal of paediatric dentistry. 2007;17(4):239-47.	Excluded by title
24	Marks LA, van Amerongen WE, Kreulen CM, Weerheijm KL, Martens LC. Conservative interproximal box-only polyacid modified composite restorations in primary molars, twelve-month clinical results. ASDC journal of dentistry for children. 1999;66(1):23-9, 12.	Excluded by title
25	Athanassouli I, Mamai-Homata E, Panagopoulos H, Koletsi-Kounari H, Apostolopoulos A. Dental caries changes between 1982 and 1991 in children aged 6-12 in Athens, Greece. Caries Res 1994;28(5):378-82.	Excluded by abstract
26	Bravo Perez M, Llodra Calvo JC, Baca Garcia P, Osorio Ruiz E, Junco Lafuente P. [Fissure sealants versus fluorine varnish on the first permanent molars: economic assessment]. Atencion primaria. 1995;15(3):143-7.	Excluded by abstract
27	Choudhary P, Tandon S, Ganesh M, Mehra A. Evaluation of the remineralization potential of amorphous calcium phosphate and fluoride containing pit and fissure sealants using scanning electron microscopy. Indian journal of dental research : official publication of Indian Society for Dental Research. 2012;23(2):157-63.	Excluded by abstract
28	Holst A, Braune K, Kjellberg M. Changes in caries experience among 6-year-olds in Blekinge, Sweden between 1994 and 2000. Swedish Dental Journal. 2004;28(3):129-35.	Excluded by abstract
29	Jensen O, Billings R, Featherstone J. Clinical evaluation of Fluroshield pit and fissure sealant. Clinical preventive dentistry [Internet]. 1990; 12(4):[24-7 pp.].	Excluded by abstract
30	Kulkami SS, Deshpande SD. Caries prevalence and treatment needs in 11-15 year old children of Belgaum city. Journal of the Indian Society of Pedodontics and Preventive Dentistry. 2002;20(1):12-5.	Excluded by abstract
31	Liu Y, Rong W, Zhao X, Wang M, Jiang Q, Wang W. [Caries prevention effect of resin based sealants and glass ionomor sealants]. Zhonghua kou qiang yi xue za zhi = Zhonghua kouqiang yixue zazhi = Chinese journal of stomatology. 2014;49(4):199-203.	Excluded by abstract

32	Mellor AC, Blinkhorn AS, Hassall DC, Holloway PJ, Worthington HV. An assessment of capitation in the General Dental Service Contract 2. Patterns of treatment provided to regularly attending patients. British Dental Journal. 1997;182(12):460-4.	Excluded by abstract
33	Morgan MV, Adams GG, Campain AC, Wright FAC. Assessing sealant retention using a Poisson frailty model. Community Dental Health. 2005;22(4):237-45.	Excluded by abstract
34	Nilchian F, Rodd HD, Robinson PG. The success of fissure sealants placed by dentists and dental care professionals. Community Dental Health. 2011;28(1):99-103.	Excluded by abstract
35	Pinar A, Sepet E, Aren G, Bolukbasi N, Ulukapi H, Turan N. Clinical performance of sealants with and without a bonding agent. Quintessence international (Berlin, Germany : 1985). 2005;36(5):355-60.	Excluded by abstract
36	Poulsen P. Retention of glassionomer sealant in primary teeth in young children. European journal of paediatric dentistry : official journal of European Academy of Paediatric Dentistry. 2003;4(2):96-8.	Excluded by abstract
37	Simonsen RJ. Retention and effectiveness of a single application of white sealant after 10 years. The Journal of the American Dental Association. 1987;115(1):31-6.	Excluded by abstract
38	Virtanen JI, Forsberg H, Ekman A. Timing and effect of fissure sealants on permanent molars: A study in Finland and Sweden. Swedish Dental Journal. 2003;27(4):159-65.	Excluded by abstract
39	Wyne AH. Caries prevalence, severity, and pattern in preschool children. Journal of Contemporary Dental Practice. 2008;9(3):024-31.	Excluded by abstract
40	Ekstrand KR, Bakhshandeh A, Martignon S. Treatment of proximal superficial caries lesions on primary molar teeth with resin infiltration and fluoride varnish versus fluoride varnish only: efficacy after 1 year. Caries Res 2010;44(1):41-6.	Excluded; no sealant used
41	Jensen SS, Nattestad A, Egdo P, Sewerin I, Munksgaard EC, Schou S. A prospective, randomized, comparative clinical study of resin composite and glass ionomer cement for retrograde root filling. Clinical oral investigations. 2002;6(4):236-43.	Excluded; no sealant used
42	Lee W, Spiekerman C, Heima M, Eggertsson H, Ferretti G, Milgrom P, et al. The effectiveness of xylitol in a school-based cluster-randomized clinical trial. Caries Res 2015;49(1):41-9.	Excluded; no sealant used
43	Lenzi TL, Menezes LBR, Soares FZM, Rocha RO. Effect of air abrasion and polishing on primary molar fissures. European Archives of Paediatric Dentistry. 2013;14(2):117-20.	Excluded; no sealant used
44	Lo ECM, Luo Y, Fan MW, Wei SHY. Clinical investigation of two glass-ionomer restoratives used with the atraumatic restorative treatment approach in China: Two-years results. Caries Res 2001;35(6):458-63.	Excluded; no sealant used
45	Roshan NM, Sakeenabi B. Survival of occlusal ART restorations in primary molars placed in school environment and hospital dental setup-one year follow-up study. Medicina Oral Patologia Oral Y Cirugia Bucal. 2011;16(7):C973-C7.	Excluded; no sealant used
46	Yee R. An ART field study in western Nepal. International Dental Journal. 2001;51(2):103-8.	Excluded; no sealant used
47	Wang X, Wang B, Wang Y. Antibacterial orthodontic cement to combat biofilm and white spot lesions. American Journal of Orthodontics and Dentofacial Orthopedics. 2015;148(6):974-81.	Excluded; no sealant used
48	Agustsdottir H, Gudmundsdottir H, Eggertsson H, Jonsson SH, Gudlaugsson JO, Saemundsson SR, et al. Caries prevalence of permanent teeth: A national survey of children in Iceland using ICDAS. Community Dent Oral Epidemiol 2010;38(4):299-309.	Excluded; no RCT
49	Bachanek T, Hendze B, Komsta A, Wolańska E. Health condition and treatment needs of mineralized tissues of permanent teeth in 7-year-old children from the Lublin region. Dental and Medical Problems. 2015;52(1):47-53.	Excluded; no RCT
50	Blinkhorn AS, Hassall DC, Holloway PJ, Mellor AC, Worthington HV. An assessment of capitation in the new General Dental Service contract. Community Dental Health. 1996;13 SUPPL. 1:3-20.	Excluded; no RCT
51	Borsatto MC, Corona SAM, Ramos RP, Liporaci Jr JLJ, Pécora JD, Palma-Dibb RG. Microleakage at sealant/enamel interface of primary teeth: Effect of Er:YAG laser ablation of pits and fissures. Journal of Dentistry for Children. 2004;71(2):143-7.	Excluded; no RCT
52	Chestnutt IG, Chadwick BL, Hutchings S, Playle R, Pickles T, Lisles C, et al. Protocol for "Seal or Varnish?" (SoV) trial: a randomised controlled trial to measure the relative cost and effectiveness of pit and fissure sealants and fluoride varnish in preventing dental decay. BMC oral health. 2012;12:51.	Excluded; no RCT
53	Collette J, Wilson S, Sullivan D. A study of the Isolite system during sealant placement: efficacy and patient acceptance. Pediatr Dent 2010;32(2):146-50.	Excluded; no RCT
54	Ekstrand KR, Martignon S, Christiansen MEC. Frequency and distribution patterns of sealants among 15-year-olds in Denmark in 2003. Community Dental Health. 2007;24(1):26-30.	Excluded; no RCT
55	Evans RW, Dennison PJ. The Caries Management System: an evidence-based preventive strategy for dental practitioners. Application for children and adolescents. Australian Dental Journal. 2009;54(4):381-9.	Excluded; no RCT
56	Folke BD, Walton JL, Feigal RJ. Occlusal sealant success over ten years in a private practice: comparing longevity of sealants placed by dentists, hygienists, and assistants. Pediatr Dent. 2004 Sep-Oct;26(5):426-32.	Excluded; no RCT
57	Holloway PJ, Blinkhorn AS, Hassall DC, Mellor AC, Worthington HV. An assessment of capitation in the General Dental Service Contract 1. The level of caries and its treatment in regularly attending children and adolescents. British Dental Journal. 1997;182(11):418-23.	Excluded; no RCT
58	Innes NP, Clarkson JE, Speed C, Douglas GV, Maguire A. The FiCTION dental trial protocol - filling children's teeth: indicated or not? BMC oral health. 2013;13:25.	Excluded; no RCT
59	Knobloch LA, Meyer T, Kerby RE, Johnston W. Microleakage and bond strength of sealant to primary enamel comparing air abrasion and acid etch techniques. Pediatr Dent 2005;27(6):463-9.	Excluded; no RCT
60	Selwitz RH, Nowjack-Raymer R, Driscoll WS, Li SH. Evaluation after 4 years of the combined use of fluoride and dental sealants. Community Dent Oral Epidemiol 1995;23(1):30-5.	Excluded; no RCT
61	Srinivasan V, Deery C, Nugent Z. In-vitro microleakage of repaired fissure sealants: a randomized, controlled trial. International journal of paediatric dentistry. 2005;15(1):51-60.	Excluded; no RCT
62	Tellez M, Gray SL, Gray S, Lim S, Ismail AI. Sealants and dental caries: Dentists' perspectives on evidence-based recommendations. Journal of the American Dental Association. 2011;142(9):1033-40.	Excluded; no RCT
63	Tirali RE, Celik C, Arhun N, Berk G, Cehreli SB. Effect of Laser and Air Abrasion Pretreatment on the Microleakage of a Fissure Sealant Applied with Conventional and Self Etch Adhesives. Journal of Clinical Pediatric Dentistry. 2013;37(3):281-8.	Excluded; no RCT
64	Tiwari T. A School-Based Lay Workforce Model Reduced Dental Caries Incidence in Children. Journal of Evidence-Based Dental Practice. 2016;16(3):196-8.	Excluded; no RCT

65	Vrbič V. Retention of a fluoride-containing sealant on primary and permanent teeth 3 years after placement. Quintessence International. 1999;30(12):825-8.	Excluded; no RCT
66	van Wyk PJ, Kroon J, White JG. Evaluation of a fissure sealant program as part of community-based teaching and training. J Dent Educ 2004;68(1):50-4.	Excluded; no RCT
67	Ammari MM, Soviero VM, Da Silva Fidalgo TK, Lenzi M, Ferreira DMTP, Mattos CT, et al. Is non-cavitated proximal lesion sealing an effective method for caries control in primary and permanent teeth? A systematic review and meta-analysis. Journal of dentistry. 2014;42(10):1217-27.	Excluded; SR
68	James P, Parnell C, Whelton H. The caries-preventive effect of chlorhexidine varnish in children and adolescents: A systematic review. Caries Res 2010;44(4):333-40.	Excluded; SR
69	Mejàre I, Lingström P, Petersson LG, Holm AK, Twetman S, Källestål C, et al. Caries-preventive effect of fissure sealants: A systematic review. Acta odontologica Scandinavica. 2003;61(6):321-30.	Excluded; SR
70	Schwendicke F, Jäger AM, Paris S, Hsu LY, Tu YK. Treating pit-and-fissure caries: A systematic review and network meta-analysis. J Dent Res 2015;94(4):522-33.	Excluded; SR
71	Botton G, Morgental CS, Scherer MM, Lenzi TL, Montagner AF, Rocha RD. Are self-etch adhesive systems effective in the retention of occlusal sealants? A systematic review and meta-analysis. Int J Paediatr Dent 2016;26(6):402-11.	Excluded; SR
72	Petersson LG, Twetman S, Dahlgren H, Norlund A, Holm AK, Nordenram G, et al. Professional fluoride varnish treatment for caries control: a systematic review of clinical trials. Acta odontologica Scandinavica. 2004;62(3):170-6.	Excluded; SR
73	Wright JT, Tampi MP, Graham L, Estrich C, Crall JJ, Fontana M, et al. Sealants for preventing and arresting pit-and-fissure occlusal caries in primary and permanent molars A systematic review of randomized controlled trials-a report of the American Dental Association and the American Academy of Pediatric Dentistry. Journal of the American Dental Association. 2016;147(8):631-+.	Excluded; SR
74	Wright JT, Tampi MP, Graham L, Estrich C, Crall JJ, Fontana M, et al. Sealants for Preventing and Arresting Pit-and-fissure Occlusal Caries in Primary and Permanent Molars A systematic review of randomized controlled trials-a report of the American Academy of Pediatric Dentistry and the American Dental Association. Pediatr Dent 2016;38(4):282-94.	Excluded; SR
75	Wright JT, Crall JJ, Fontana M, Gillette EJ, Novy BB, Dhar V, et al. Evidence-based clinical practice guideline for the use of pit-and-fissure sealants A report of the American Dental Association and the American Academy of Pediatric Dentistry. Journal of the American Dental Association. 2016;147(8):672-+.	Excluded; SR
76	Ansari G, Oloomi K, Eslami B. Microleakage assessment of pit and fissure sealant with and without the use of pumice prophylaxis. International journal of paediatric dentistry. 2004;14(4):272-8.	Excluded; no teeth comparison
77	Antonson SA, Antonson DE, Brener S, Crutchfield J, Larumbe J, Michaud C, et al. Twenty-four month clinical evaluation of fissure sealants on partially erupted permanent first molars: glass ionomer versus resin-based sealant. J Am Dent Assoc 2012;143:115-22.	Excluded; no teeth comparison
78	Baginska J, Rodakowska E, Milewski R, Kierklo A. Dental caries in primary and permanent molars in 7-8-year-old schoolchildren evaluated with Caries Assessment Spectrum and Treatment (CAST) index. BMC oral health. 2014;14(1).	Excluded; no teeth comparison
79	Barja-Fidalgo F, Maroun S, de Oliveira BH. Effectiveness of a glass ionomer cement used as a pit and fissure sealant in recently erupted permanent first molars. Journal of dentistry for children (Chicago, Ill). 2009;76(1):34-40.	Excluded; no teeth comparison
80	Baseggio W, Naufel FS, Davidoff DC, Nahsan FP, Flury S, Rodrigues JA. Caries-preventive efficacy and retention of a resin-modified glass ionomer cement and a resin-based fissure sealant: a 3-year split-mouth randomised clinical trial. Oral health & preventive dentistry. 2010;8(3):261-8.	Excluded; no teeth comparison
81	Beiruti N, Frencken JE, van't Hof MA, Taifour D, van Palenstein Helderman WH. Caries-preventive effect of a one-time application of composite resin and glass ionomer sealants after 5 years. Caries Res 2006;40(1):52-9.	Excluded; no teeth comparison
82	Borges BC, De Souza Bezerra Araujo RF, Dantas RF, De Araujo Lucena A, De Assuncao Pinheiro IV. Efficacy of a non-drilling approach to manage non-cavitated dentin occlusal caries in primary molars: a 12-month randomized controlled clinical trial. International journal of paediatric dentistry. 2012;22(1):44-51.	Excluded; no teeth comparison
83	Braga MM, Mendes FM, De Benedetto MS, Imparato JCP. Effect of silver diammine fluoride on incipient caries lesions in erupting permanent first molars: A pilot study. Journal of Dentistry for Children. 2009;76(1):28-33.	Excluded; no teeth comparison
84	Bravo M, Baca P, Llodra JC, Osorio E. A 24-month study comparing sealant and fluoride varnish in caries reduction on different permanent first molar surfaces. Journal of public health dentistry. 1997;57(3):184-6.	Excluded; no teeth comparison
85	Bravo M, Garcia-Anllo I, Baca P, Llodra JC. A 48-month survival analysis comparing sealant (Delton) with fluoride varnish (Duraphat) in 6- to 8-year-old children. Community Dent Oral Epidemiol 1997;25(3):247-50.	Excluded; no teeth comparison
86	Bravo M, Llodra JC, Baca P, Osorio E. Effectiveness of visible light fissure sealant (Delton) versus fluoride varnish (Duraphat): 24-month clinical trial. Community Dent Oral Epidemiol 1996;24(1):42-6.	Excluded; no teeth comparison
87	Bravo M, Montero J, Bravo JJ, Baca P, Llodra JC. Sealant and fluoride varnish in caries: a randomized trial. J Dent Res 2005;84(12):1138-43.	Excluded; no teeth comparison
88	Cagetti MG, Carta G, Cocco F, Sale S, Congiu G, Mura A, et al. Effect of Fluoridated Sealants on Adjacent Tooth Surfaces: A 30-mo Randomized Clinical Trial. J Dent Res 2014;93(7 Suppl):59s-65s.	Excluded; no teeth comparison
89	Chadwick BL, Treasure ET, Playle RA. A randomised controlled trial to determine the effectiveness of glass ionomer sealants in pre-school children. Caries Res 2005;39(1):34-40.	Excluded; no teeth comparison
90	Chen X, Liu X. Clinical comparison of Fuji VII and a resin sealant in children at high and low risk of caries. Dental materials journal. 2013;32(3):512-8.	Excluded; no teeth comparison
91	De Menezes Abreu DM, Leal SC, Mulder J, Frencken JE. Dental anxiety in 6-7-year-old children treated in accordance with conventional restorative treatment, ART and ultra-conservative treatment protocols. Acta odontologica Scandinavica. 2011;69(6):410-6.	Excluded; no teeth comparison
92	Guler C, Yilmaz Y. A two-year clinical evaluation of glass ionomer and ormocer based fissure sealants. The Journal of clinical pediatric dentistry. 2013;37(3):263-7.	Excluded; no teeth comparison
93	Gungor HC, Altay N, Alpar R. Clinical evaluation of a polyacid-modified resin composite-based fissure sealant: two-year results. Operative dentistry. 2004;29(3):254-60.	Excluded; no teeth comparison
94	Hesse D, Bonifacio CC, Mendes FM, Braga MM, Imparato JC, Raggio DP. Sealing versus partial caries removal in primary	Excluded; no teeth

	molars: a randomized clinical trial. BMC oral health. 2014;14:58.	comparison
95	Kanellis MJ, Warren JJ, Levy SM. A comparison of sealant placement techniques and 12-month retention rates. Journal of public health dentistry. 2000;60(1):53-6.	Excluded; no teeth comparison
96	Kervanto-Seppala S, Lavonius E, Pietila I, Pitkaniemi J, Meurman JH, Kerosuo E. Comparing the caries-preventive effect of two fissure sealing modalities in public health care: a single application of glass ionomer and a routine resin-based sealant programme. A randomized split-mouth clinical trial. International journal of paediatric dentistry. 2008;18(1):56-61.	Excluded; no teeth comparison
97	Khatri SG, Samuel SR, Acharya S, Patil S, Madan K. Retention of Moisture-tolerant and Conventional Resin-based Sealant in Six- to Nine-year-old Children. Pediatr Dent 2015;37(4):366-70.	Excluded; no teeth comparison
98	Kucukyilmaz E, Savas S. Evaluation of Different Fissure Sealant Materials and Flowable Composites Used as Pit-and-fissure Sealants: A 24-Month Clinical Trial. Pediatr Dent 2015;37(5):468-73.	Excluded; no teeth comparison
99	Li S-F, Deng M, He G-Q, Luo W-N. [Evaluating the effects of GcFuji II glass ionomer cement in pit and fissure enameloplasty sealant technique]. Journal of Clinical Rehabilitative Tissue Engineering Research [Internet]. 2008; 12(23):[4457-60 pp.].	Excluded; no teeth comparison
100	Lygidakis NA, Dimou G, Stamataki E. Retention of fissure sealants using two different methods of application in teeth with hypomineralised molars (MIH): a 4 year clinical study. European archives of paediatric dentistry : official journal of the European Academy of Paediatric Dentistry. 2009;10(4):223-6.	Excluded; no teeth comparison
101	Maher MM, Elkashlan HI, El-Housseiny AA. Effectiveness of a self-etching adhesive on sealant retention in primary teeth. Pediatr Dent 2013;35(4):351-4.	Excluded; no teeth comparison
102	Martignon S, Tellez M, Santamaria RM, Gomez J, Ekstrand KR. Sealing distal proximal caries lesions in first primary molars: efficacy after 2.5 years. Caries Res 2010;44(6):562-70.	Excluded; no teeth comparison
103	Monse B, Heinrich-Weltzien R, Mulder J, Holmgren C, van Palenstein Helderman WH. Caries preventive efficacy of silver diammine fluoride (SDF) and ART sealants in a school-based daily fluoride toothbrushing program in the Philippines. BMC oral health. 2012;12:52.	Excluded; no teeth comparison
104	Muller-Bolla M, Pierre A, Lupi-Pegurier L, Velly AM. Effectiveness of school-based dental sealant programs among children from low-income backgrounds: a pragmatic randomized clinical trial with a follow-up of 3 years. Community Dent Oral Epidemiol 2016;44(5):504-11.	Excluded; no teeth comparison
105	Nogourani MK, Janghorbani M, Khadem P, Jadidi Z, Jalali S. A 12-month clinical evaluation of pit-and-fissure sealants placed with and without etch-and-rinse and self-etch adhesive systems in newly-erupted teeth. Journal of applied oral science : revista FOB. 2012;20(3):352-6.	Excluded; no teeth comparison
106	Oulis CJ, Tsinidou K, Vadiakas G, Mamai-Homata E, Polychronopoulou A, Athanasouli T. Caries prevalence of 5, 12 and 15-year-old Greek children: A national pathfinder survey. Community Dental Health. 2012;29(1):29-32.	Excluded; no teeth comparison
107	Pereira AC, Pardi V, Mialhe FL, Meneghim MC, Basting RT, Werner CW. Clinical evaluation of a polyacid-modified resin used as a fissure sealant: 48-month results. American journal of dentistry. 2000;13(6):294-6.	Excluded; no teeth comparison
108	Poulsen S, Peltoniemi AL. Retention of fissure sealant in primary second molars after 6 months. Scandinavian Journal of Dental Research. 1979;87(4):328-30.	Excluded; no teeth comparison
109	Raadal M, Utkilen AB, Nilsen OL. Fissure sealing with a light-cured resin-reinforced glass-ionomer cement (Vitrebond) compared with a resin sealant. International journal of paediatric dentistry. 1996;6(4):235-9.	Excluded; no teeth comparison
110	Tagliaferro EP, Pardi V, Ambrosano GM, Meneghim Mde C, da Silva SR, Pereira AC. Occlusal caries prevention in high and low risk schoolchildren. A clinical trial. American journal of dentistry. 2011;24(2):109-14.	Excluded; no teeth comparison
111	Tai BJ, Jiang H, Du MQ, Peng B. Assessing the effectiveness of a school-based oral health promotion programme in Yichang City, China. Community Dent Oral Epidemiol 2009;37(5):391-8.	Excluded; no teeth comparison
112	Tang LH, Shi L, Yuan S, Lv J, Lu HX. [Effectiveness of 3 different methods in prevention of dental caries in permanent teeth among children]. Shanghai kou qiang yi xue = Shanghai journal of stomatology. 2014;23(6):736-9.	Excluded; no teeth comparison
113	Trachtenberg F, Maserejian NN, Soncini JA, Hayes C, Tavares M. Does fluoride in compomers prevent future caries in children? J Dent Res 2009;88(3):276-9.	Excluded; no teeth comparison
114	Tripodi D, Filippakos A, Piattelli A, D'Ercole S, Perrotti V. Wear of dental sealing materials using the replication technique. European journal of paediatric dentistry : official journal of European Academy of Paediatric Dentistry. 2011;12(2):95-8.	Excluded; no teeth comparison
115	Ulusu T, Odabas ME, Tuzuner T, Baygin O, Sillelioglu H, Deveci C, et al. The success rates of a glass ionomer cement and a resin-based fissure sealant placed by fifth-year undergraduate dental students. European archives of paediatric dentistry : official journal of the European Academy of Paediatric Dentistry. 2012;13(2):94-7.	Excluded; no teeth comparison
116	Veitz-Keenan A, Barna JA, Strober B, Matthews AG, Collie D, Vena D, et al. Treatments for hypersensitive noncarious cervical lesions: a Practitioners Engaged in Applied Research and Learning (PEARL) Network randomized clinical effectiveness study. Journal of the American Dental Association (1939). 2013;144(5):495-506.	Excluded; no teeth comparison
117	Weerheijm KL, Kreulen CM, Gruythuysen RJ. Comparison of retentive qualities of two glass-ionomer cements used as fissure sealants. ASDC journal of dentistry for children. 1996;63(4):265-7.	Excluded; no teeth comparison
118	Kervanto-Seppala S, Lavonius E, Kerosuo E, Pietila I. Can Glass ionomer sealants be cost-effective? The Journal of clinical dentistry. 2000;11(1):1-3.	Excluded; no eligible outcome
119	Lim S, Julliard K. Evaluating the efficacy of EMLA topical anesthetic in sealant placement with rubber dam. Pediatr Dent 2004;26(6):497-500.	Excluded; no eligible outcome
	Decision pending	
120	Coelho A. Selantes de fissura com sistemas adesivos de auto-condicionamento : estudo clínico e laboratorial. Doctoral Dissertation, University of Lisbon, 2011.	Raw data needed; requested; response pending
121	Ganesh M, Tandon S. Clinical evaluation of FUJI VII sealant material. The Journal of clinical pediatric dentistry. 2006;31(1):52-7.	Raw data needed; requested; response pending
122	Liu BY, Xiao Y, Chu CH, Lo EC. Glass ionomer ART sealant and fluoride-releasing resin sealant in fissure caries prevention--results from a randomized clinical trial. BMC oral health. 2014;14:54.	Raw data needed; requested; response pending
123	Lyman T, Viswanathan K, McWhorter A. Isolite vs cotton roll isolation in the placement of dental sealants. Pediatr Dent 2013;35(3):E95-9.	Raw data needed; requested; response pending

Included		
124	Baca P, Bravo M, Baca AP, Jimenez A, Gonzalez-Rodriguez MP. Retention of three fissure sealants and a dentin bonding system used as fissure sealant in caries prevention: 12-month follow-up results. Medicina oral, patologia oral y cirugia bucal. 2007;12(6):E459-63.	Included
125	Bhushan U, Goswami M. Evaluation of retention of pit and fissure sealants placed with and without air abrasion pretreatment in 6-8 year old children - An in vivo study. J Clin Exp Dent. 2017 Feb 1;9(2):e211-e217.	Included
126	Corona SA, Borsatto MC, Garcia L, Ramos RP, Palma-Dibb RG. Randomized, controlled trial comparing the retention of a flowable restorative system with a conventional resin sealant: one-year follow up. International journal of paediatric dentistry. 2005;15(1):44-50.	Included
127	de Oliveira DC, Cunha RF. Comparison of the caries-preventive effect of a glass ionomer sealant and fluoride varnish on newly erupted first permanent molars of children with and without dental caries experience. Acta odontologica Scandinavica. 2013;71(3-4):972-7.	Included
128	Erdemir U, Sancakli HS, Yaman BC, Ozel S, Yucel T, Yildiz E. Clinical comparison of a flowable composite and fissure sealant: a 24-month split-mouth, randomized, and controlled study. Journal of dentistry. 2014;42(2):149-57.	Included
129	Grande RH, de Lima AC, Rodrigues Filho LE, Witzel MF. Clinical evaluation of an adhesive used as a fissure sealant. Am J Dent. 2000 Aug;13(4):167-70.	Included
130	Handelman SL, Leverett DH, Espeland M, Curzon J. Retention of sealants over carious and sound tooth surfaces. Community Dent Oral Epidemiol 1987;15(1):1-5.	Included
131	Honkala S, ElSalhy M, Shyama M, Al-Mutawa SA, Boodai H, Honkala E. Sealant versus Fluoride in Primary Molars of Kindergarten Children Regularly Receiving Fluoride Varnish: One-Year Randomized Clinical Trial Follow-Up. Caries Res. 2015;49(4):458-66.	Included
132	Jodkowska E. Efficacy of pit and fissure sealing: long-term clinical observations. Quintessence international (Berlin, Germany : 1985). 2008;39(7):593-602.	Included
133	Karaman E, Yazici AR, Baseren M, Gorucu J. Comparison of Acid Versus Laser Etching on the Clinical Performance of a Fissure Sealant: 24-Month Results. Operative dentistry. 2013;38(2):151-8.	Included
134	Li SH, Swango PA, Gladsden AN, Heifetz SB. Evaluation of the retention of two types of pit and fissure sealants. Community Dent Oral Epidemiol 1981;9(4):151-8.	Included
135	Liu BY, Lo EC, Chu CH, Lin HC. Randomized trial on fluorides and sealants for fissure caries prevention. J Dent Res 2012;91(8):753-8.	Included
136	Muller-Bolla M, Lupi-Pegurier L, Bardakjian H, Velly AM. Effectiveness of school-based dental sealant programs among children from low-income backgrounds in France: a pragmatic randomized clinical trial. Community Dent Oral Epidemiol 2013;41(3):232-41.	Included
137	Poulsen S, Beiruti N, Sadat N. A comparison of retention and the effect on caries of fissure sealing with a glass-ionomer and a resin-based sealant. Community Dent Oral Epidemiol 2001;29(4):298-301.	Included
138	Qvist V, Borum MK, Moller KD, Andersen TR, Blanche P, Bakhshandeh A. Sealing Occlusal Dentin Caries in Permanent Molars:7-Year Results of a Randomized Controlled Trial. JDR Clin Translat Res 2017;2(1):73-86.	Included
139	Sgavioli CAPP. Clinical evaluation of the retention of sealant depending on the posterior application or non-application of fluoride after sealing. Master Thesis, Sao Paolo University, 2000.	Included

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Appendix 3. Communication attempts with trialists.

Nr	Paper	Contact details	Contact reason	Status
1	Coelho A. Selantes de fissura com sistemas adesivos de auto-condicionamento : estudo clínico e laboratorial. Doctoral Dissertation, University of Lisbon, 2011.	Ana Carla Rodrigues Sousa Coelho Canta; Private clinic Joao Pedro Canta, Moita, Portugal.	SL data	Pending.
2	Honkala S, ElSalhy M, Shyama M, Al-Mutawa SA, Boodai H, Honkala E. Sealant versus Fluoride in Primary Molars of Kindergarten Children Regularly Receiving Fluoride Varnish: One-Year Randomized Clinical Trial Follow-Up. Caries Res. 2015;49(4):458-66.	Sisko Honkala; Faculty of Dentistry, Kuwait University, Safat, Kuwait.	SL data; excluding varnish	Responded (18 April); sent raw data.
3	Liu BY, Lo EC, Chu CH, Lin HC. Randomized trial on fluorides and sealants for fissure caries prevention. J Dent Res 2012;91(8):753-8.	Edward C.M. Lo; Faculty of Dentistry, The University of Hong Kong, 34 Hospital Road, Hong Kong.	SL data; excluding SDF/NaF	Responded (18 April); sent raw data.
4	Liu BY, Xiao Y, Chu CH, Lo EC. Glass ionomer ART sealant and fluoride-releasing resin sealant in fissure caries prevention--results from a randomized clinical trial. BMC oral health. 2014;14:54.	Bao Ying Liu; Faculty of Dentistry, The University of Hong Kong, 34 Hospital Road, Hong Kong.	SL data; excluding SDF/NaF	Pending.
5	Lyman T, Viswanathan K, McWhorter A. Isolite vs cotton roll isolation in the placement of dental sealants. Pediatr Dent 2013;35(3):E95-9.	Kavitha Viswanathan; Department of Pediatric Dentistry, Texas A&M University, Baylor College of Dentistry, Dallas, Texas, USA.	SL data	Pending.
6	Poulsen S, Beiruti N, Sadat N: A comparison of retention and the effect on caries of fissure sealing with a glass-ionomer and a resin-based sealant. Community Dent Oral Epidemiol 2001; 29: 298–301	Sven Poulsen; Department of Community Oral Health and Pediatric Dentistry, Royal Dental College, Faculty of Health Sciences, University of Aarhus, Aarhus, Denmark.	SL data	Responded (25 April); sent aggregate data.
7	Ganesh M, Tandon S. Clinical evaluation of FUJI VII sealant material. The Journal of clinical pediatric dentistry. 2006;31(1):52-7.	M. Ganesh; Dept. of Pedodontics & Preventive Dentistry, Manipal College of Dental Sciences, Karnataka, India.	SL data	Pending.

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Appendix 4. Risk of bias of included trials.

Study ID	Sequence generation	Allocation concealment	Blinding of participants/ personnel	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting	Other sources of bias
Baca 2007	Unclear – unclear description: 'All four materials were used in every child in the study, with a different material randomly applied to each quadrant.'	Unclear – no information provided	Unclear – blinding impractical, but outcome objective and outcome assessor blinded.	Low risk – blinding attempt judged as adequate: 'Colored glasses were worn by the clinician to minimize sealant color differences, guaranteeing a blind examination'	Low risk – low drop-out rate (16.4%); however, trial is split-mouth, so drop-outs are expected to be evenly distributed.	Unclear – not clear as no protocol/registration available.	Low risk – group comparatibiliy and co-interventions judged similar due to the trial's split-mouth nature.
Bhushan 2017	High risk – non-random allocation: 'The right maxillary and mandibular primary 2nd molars and permanent 1st molars (Group A) were treated by acid etching alone whilethe left maxillary and mandibular primary 2nd molars and permanent 1st molars were pretreated with air abrasion followed by acid etching (Group B) before application of pit and fissure sealant.'	Unclear – no information provided	Unclear – blinding impractical, but outcome objective and outcome assessor blinded.	Low risk – blinding attempt judged as adequate: 'Subjects were clinically evaluated after 3 and 6 months of sealant placement by study supervisor as a blinded outcome assessor.'	Low risk – low drop-out rate (14.0%); however, trial is split-mouth, so drop-outs are expected to be evenly distributed.	Unclear – not clear as no protocol/ registration available.	Low risk – group comparatibiliy and co-interventions judged similar due to the trial's split-mouth nature.
Corona 2005	Unclear – 'Using a half-mouth design, a filled resin-based pit-and-fissure sealant (…),was applied on randomly assigned upper/ lower primary and permanent molars of one side of the mouth, and a single-bottle adhesive system (…) used in association with a flowable resin composite (…) was applied to the contra-lateral side.'	Unclear – no information provided	High risk – blinding impractical and no blinding of outcome assessor.	High risk – no blinding reported.	Low risk – although somewhat unclear, probably no drop-outs.	Unclear – not clear as no protocol/ registration available.	Low risk – group comparatibiliy and co-interventions judged similar due to the trial's split-mouth nature.
de Oliveira 2013	High risk – non-random allocation: 'The glass ionomer sealant was applied to the right maxillary and mandibular first molars. The fluoride varnish was applied to the left maxillary and mandibular first molars in three sessions.'	Unclear – no information provided	High risk – blinding impractical and no blinding of outcome assessor.	High risk – no blinding reported.	Low risk – low drop-out rate (6.6%); however, trial is split-mouth, so drop-outs are expected to be evenly distributed.	Unclear – not clear as no protocol/ registration available.	Low risk – group comparatibiliy and co-interventions judged similar due to the trial's split-mouth nature.
Erdemir 2014	Low risk – 'The placement of the materials at the right/left side of the mouth was randomized using a contingency number table.'	Unclear – no information provided	Unclear – blinding impractical, but outcome objective and outcome assessor blinded.	Low risk – blinding attempt judged as adequate: 'Each restoration was independently evaluated using a mirror, blunt explorer, and air stream at baseline (…) and at 1, 6, 12, and 24 months by 2 calibrated investigators, who were not involved with the treatment procedures.'	Low risk – low drop-out rate (12.7%); however, trial is split-mouth, so drop-outs are expected to be evenly distributed.	Unclear – not clear as no protocol/ registration available.	Low risk – group comparatibiliy and co-interventions judged similar due to the trial's split-mouth nature.
Grande 2000	High risk – non-random allocation: 'For the first volunteer, the side of the mouth to receive a given material was randomized and for the others, the assignment was done alternately.'	Unclear – no information provided	High risk – blinding impractical and no blinding of outcome assessor.	High risk – no blinding reported.	Unclear – no information on drop-out rate; however, trial is split-mouth, so drop-outs are expected to be evenly distributed.	Unclear – not clear as no protocol/ registration available.	Low risk – group comparatibiliy and co-interventions judged similar due to the trial's split-mouth nature.
Handelman 1987	Unclear – 'On a random basis, an autopolymerizing resin without a filler (...) or an ultraviolet light activated resin with a filler (...) was placed by a single operator on the occlusal surfaces of all permanent molars and premolars on one side of the mouth, with the other sealant on the contralateral side.'	Unclear – no information provided	Unclear – blinding impractical, but outcome objective and outcome assessor blinded.	Low risk – blinding attempt judged as adequate: 'Two trained and calibrated dentists (not the operator) examined all subjects at the first and second recall visit. They had no knowledge of initial caries diagnosis, the type of sealant or, at the time of the second examination, whether the tooth had been resealed after the first recall examination.'	Unclear – no information on drop-out rate; however, trial is split-mouth, so drop-outs are expected to be evenly distributed.	Unclear – not clear as no protocol/ registration available.	Low risk – group comparatibiliy and co-interventions judged similar due to the trial's split-mouth nature.
Honkala 2015	Low risk – 'Clinical files of these children were numbered with continuous numbers, and eligible quadrant pairs were then randomized to the intervention by S.H. using computerized random numbers.'	Low risk – allocation by a separate person not involved to clinical procedures.	Unclear – blinding impractical, but outcome objective and outcome assessor blinded.	Low risk – blinding attempt judged as adequate: 'The examiner had no information which molar had sealant/ varnish/no intervention.'	Low risk – no drop outs: 'All treated matched molar surfaces could be examined after 1 year.'	Low risk – all outcomes specified in the trial protocol have been reported.	Low risk – group comparatibiliy and co-interventions judged similar due to the trial's split-mouth nature.
Jodkowska 2008	Unclear – unclear description: 'Teeth designated for sealing were allotted at random to be sealed with 1 of the materials used.'	Unclear – no information provided	High risk – blinding impractical and no blinding of outcome assessor.	High risk – no blinding reported.	High risk – no information on drop-out rate; trial is split-mouth, but it is unclear whether all tested materials were used in all patients; detailed information about material drop outs are not given.	Unclear – not clear as no protocol/ registration available.	Low risk – group comparatibiliy and co-interventions judged similar due to the trial's split-mouth nature.
Karaman 2013	Low risk – 'A table of random numbers was used to assign the teeth for etching with either acid or laser.'	Unclear – no information provided	Unclear – blinding impractical, but outcome objective and outcome assessor blinded.	Low risk – blinding attempt judged as adequate: 'All patients were available for all evaluations. Two calibrated examiners, who were unaware of which preparation method had been used and who were not involved in the treatment procedures, evaluated the restorations at baseline, and at 6-, 12-, 18-, and 24-month follow-up visits.'	Low risk – no drop outs: '…all of them were available for all evaluations (total recall rate was 100%).'	Unclear – not clear as no protocol/ registration available.	Low risk – group comparatibiliy and co-interventions judged similar due to the trial's split-mouth nature.
Li 1981	Unclear – unclear description: 'Teeth on one side of the mouth of each participant were randomly assigned to be treated with Nuva-Seal; teeth on the other side were designated for treatment with Delton.'	Unclear – no information provided	Unclear – blinding impractical, but outcome objective and outcome assessor blinded.	Low risk – blinding attempt judged as adequate: '; ...however, the examiner did not know which side of the mouth received Nuva-Sela and which received Delton.'	Low risk – no specific information on overall drop-out rate; however, trial is split-mouth, so drop-outs are expected to be evenly distributed.	Unclear – not clear as no protocol/ registration available.	Low risk – group comparatibiliy and co-interventions judged similar due to the trial's split-mouth nature.
Liu 2012	Low risk – 'A coin was then thrown to decide which side of the molars would be assigned the group with a smaller group number in the combination.'	Low risk – 'Papers with the numbers written on were put into an envelope to be drawn by an assistant to decide the group combination of the included molars of a subject.'	Unclear – blinding impractical, but outcome objective and outcome assessor blinded.	Low risk – blinding attempt judged as adequate: 'Development of dentine caries (ICDAS Code 4–6) and sealant retention (…) in the molars was assessed blindly every 6 months by the same two calibrated dentists involved in the baseline examination.'	Low risk – no drop outs: 'All treated matched molar surfaces could be examined after 1 year.'	Low risk – all outcomes specified in the trial protocol have been reported.	Low risk – group comparatibiliy and co-interventions judged similar.
Muller-Bolla 2013	Low risk – 'The allocation sequence was generated using block of four by one of the authors (MMB).'	Low risk – allocation by a separate person not involved to clinical procedures.	High risk – blinding impractical and no blinding of outcome assessor.	High risk – no blinding reported.	Low risk – low drop-out rate (8.3%), which is appropriately assessed; anyway, trial is split-mouth, so drop-outs are expected to be evenly distributed.	Unclear – not clear as no protocol/ registration available.	Low risk – group comparatibiliy and co-interventions judged similar due to the trial's split-mouth nature.
Poulsen 2001	Low risk – 'In each child random numbers were used to decide which tooth should be sealed with the resin material and which tooth should be sealed with glass ionomer.'	Unclear – no information provided	High risk – blinding impractical and no blinding of outcome assessor.	High risk – no blinding reported.	Unclear – no information on drop-out rate; however, trial is split-mouth, so drop-outs are expected to be evenly distributed.	Unclear – not clear as no protocol/ registration available.	Low risk – group comparatibiliy and co-interventions judged similar due to the trial's split-mouth nature.
Qvist 2017	Low risk – 'For each clinician, computerized randomization between sealing and restoration was made at the University of Copenhagen and saved at the clinic in sequentially numbered, sealed envelopes.'	Low risk – 'Selection bias was prevented by allocation concealment until intervention was assigned'	High risk – blinding impractical and no blinding of outcome assessor.	High risk – no blinding reported.	Low risk – 'The 40 drop outs were equally distributed among sealings and restorations (P=0.43), with no significant association to predictor variables (P = 0.21 to 0.95).'	Low risk – all outcomes specified in the trial protocol have been reported.	Low risk – group comparatibiliy judged similar and taken into account in multivariate analyses.
Sgavioli 2000	Unclear – unclear description: 'The molars were randomly divided into 2 experimental groups:…'	Unclear – no information provided	High risk – blinding impractical and no blinding of outcome assessor.	High risk – no blinding reported.	Low risk – no drop outs.	Unclear – not clear as no protocol/ registration available.	Low risk – group comparatibiliy judged similar as one molar was included from each patient and patients were randomly allocated.

Appendix 5. Re-analysis of the raw data of the Liu et al., 2012 provided by the trialists.

	12 mos	24 mos		Status	n (%)	n (%)		
Tooth	n (%)	n (%)		SL total loss	78 (21.1%)	127 (34.6%)		
16	84 (22.7%)	84 (22.9%)		Caries	1 (0.3%)	7 (1.9%)		
26	85 (23.0%)	85 (23.2%)		Restoration	1 (0.3%)	4 (1.1%)		
36	99 (26.8%)	98 (26.7%)		SL total retention	49 (13.2%)	26 (7.1%)		
46	102 (27.6%)	100 (27.3%)		SL partial retention	241 (65.1%)	203 (55.3%)		
Combined loss	12 mos			24 mos				
Tooth	Retention	Fail	P	Retention	Fail	P		
16	8 (9.5%)	76 (90.5%)	0.516	6 (7.3%)	76 (92.7%)	0.519		
26	13 (15.3%)	72 (84.7%)		5 (6.0%)	79 (94.1%)			
36	16 (16.3%	82 (83.7%)		10 (10.5%)	85 (89.5%)			
46	12 (11.9%)	89 (88.1%)		5 (5.3%)	90 (94.7%)			
Only total loss	12 mos			24 mos				
Tooth	Retention	Fail	P	Retention	Fail			
16	59 (70.2%)	25 (29.8%)	0.003	46 (56.1%)	36 (43.9%)	P		
26	61 (71.8%)	24 (28.2%)		49 (58.3%)	35 (41.7%)	0.063		
36	79 (80.6%)	19 (19.4%)		65 (68.4%)	30 (31.6%)			
46	91 (90.1%)	10 (9.9%)		69 (72.6%)	26 (27.4%)			
Caries/restoration	12 mos			24 mos				
Tooth	No	Yes	P	No	Yes			
16	84 (100.0%)	0 (0%)	0.639	82 (97.6%)	2 (2.4%)	P		
26	85 (100.0%)	0 (0%)		84 (98.8%)	1 (1.2%)	0.483		
36	98 (99.0%)	1 (1.0%)		95 (96.9%)	3 (3.1%)			
46	101 (99.0%)	1 (1.0%)		95 (95.0%)	5 (5.0%)			
			12 mos			24 mos		
	Factor	Category	RR	95% CI	P	RR	95% CI	P
Combined loss	Jaw	Maxilla	Ref			Ref		
		Mandible	0.98	0.91,1.06	0.599	0.99	0.94,1.05	0.762
	Side	Right	Ref			Ref		
		Left	0.94	0.87,1.02	0.140	0.98	0.92,1.04	0.472
Only total loss	Factor	Category	RR	95% CI	P	RR	95% CI	P
	Jaw	Maxilla	Ref			Ref		
		Mandible	0.51	0.34,0.77	0.001	0.69	0.52,0.91	0.010
	Side	Right	Ref			Ref		
		Left	1.21	0.82,1.78	0.345	1.02	0.78,1.35	0.865
Caries/restoration	Factor	Category	RR	95% CI	P	RR	95% CI	P
	Jaw	Maxilla	Ref			Ref		
		Mandible	NA	NA		2.26	0.61,8.39	0.221
	Side	Right	Ref			Ref		
		Left	1.05	0.07,16.57	0.972	0.58	0.17,1.94	0.375

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Appendix 6. Re-analysis of the raw data of the Honkala et al., 2015 trial provided by the trialists – Sample demographics.

Gender	n (%)
Female	126 (47.6%)
Male	139 (52.5%)
Age	n (%)
4	249 (94.0%)
5	16 (6.0%)
Grade	n (%)
1	265 (100%)
School	n (%)
1	134 (50.6%)
2	131 (49.4%)
Tooth	n (%)
54	42 (15.9%)
55	42 (15.9%)
64	33 (12.5%)
65	28 (10.6%)
74	37 (14.0%)
75	35 (13.2%)
84	25 (9.4%)
85	23 (8.7%)
Jaw	n (%)
Maxilla	145 (54.7%)
Mandible	120 (45.3%)
Side	n (%)
Right	132 (49.8%)
Left	133 (50.2%)
Molar	n (%)
1st	137 (51.7%)
2nd	128 (48.3%)
Restoration	n (%)
Not sealed or restored	23 (8.7%)
Sealant partial	35 (13.2%)
Sealant full	204 (77.0%)

Tooth coloured restoration	2 (0.8%)
Stainless steel crown	1 (0.4%)
Carious progression	n (%)
Sound tooth surface	233 (87.9%)
First visual change in enamel	5 (1.9%)
Distinct visual change in enamel	12 (4.5%)
Dentinal shadow	13 (4.9%)
Distict cavity with visible dentin	2 (0.8%)
Combined loss	n (%)
No	204 (77.9%)
Yes	58 (22.1%)
Only total loss	n (%)
No	239 (91.2%)
Yes	23 (8.8%)
Carious lesion	n (%)
No	247 (93.2%)
Yes	18 (6.8%)

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Appendix 7. Re-analysis of the raw data of the Honkala et al., 2015 trial provided by the trialists – Inferential statistics.

	Combined loss			Only total loss			Caries		
	n (%)	n (%)		n (%)	n (%)		n (%)	n (%)	
	No	Yes	P	No	Yes	P	No	Yes	P
Jaw									
Maxilla	112 (78.3%)	31 (21.7%)	0.844	132 (92.3%)	11 (7.7%)	0.496	138 (95.2%)	7 (4.8%)	0.162
Mandible	92 (77.3%)	27 (22.7%)		107 (89.9%)	12 (10.1%)		109 (90.8%)	11 (9.2%)	
Side									
Right	103 (78.0%)	29 (22.0%)	0.947	125 (94.7%)	7 (5.3%)	0.045	127 (96.2%)	5 (3.8%)	0.053
Left	101 (77.7%)	29 (22.3%)		114 (87.7%)	16 (12.3%)		120 (90.2%)	13 (9.8%)	
Molar									
1st	109 (80.7%)	26 (19.3%)	0.247	122 (90.4%)	13 (9.6%)	0.616	128 (93.4%)	9 (6.6%)	0.881
2nd	95 (74.8%)	32 (25.2%)		117 (92.1%)	10 (7.9%)		119 (93.0%)	9 (7.0%)	

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X

		Combined loss			Only total loss			Caries		
		RR	95% CI	P	RR	95% CI	P	RR	95% CI	P
Jaw	Maxilla	Ref			Ref			Ref		
	Mandible	1.02	0.69,1.52	0.911	1.16	0.51,2.65	0.730	1.65	0.68,4.02	0.272
Side	Right	Ref			Ref			Ref		
	Left	1.01	0.68,1.49	0.972	2.26	0.91,5.60	0.079	2.37	0.96,5.82	0.060
Molar	1st	Ref			Ref			Ref		
	2nd	1.31	0.83,2.06	0.249	0.82	0.47,1.44	0.500	1.06	0.45,2.49	0.899

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Appendix 8. Results of all available data on all outcomes/timepoints reported in included studies.

	Outcome	Mos	N	RR (95% CI)	P	tau^2 (95% CI)	I^2 (95% CI)
Right side versus left side (referent)							
	Combined loss	6	2	1.07 (0.71,1.62)	0.745	0.05 (0,27.77)	39 (0,100)
	Combined loss	12	4	1.04 (0.78,1.40)	0.779	0.07 (0,0.97)	93 (0,100)
	Combined loss	24	3	1.31 (0.67,2.55)	0.433	0.32 (0.08,12.72)	99 (96,100)
	Combined loss	36	2	1.23 (0.71,2.14)	0.461	0.14 (0,0)	82 (0,0)
	Combined loss	Max	4	1.08 (0.82,1.43)	0.576	0.06 (0,0.84)	97 (0,100)
	Only total loss	6	2	1.06 (0.49,2.31)	0.877	0.18 (0,0)	38 (0,0)
	Only total loss	12	4	1.24 (0.74,2.07)	0.415	0.19 (0,1.92)	79 (0,97)
	Only total loss	24	3	1.24 (0.68,2.24)	0.483	0.23 (0,8.78)	91 (0,100)
	Only total loss	36	2	1.03 (0.78,1.38)	0.821	0.02 (0,0.87)	19 (0,91)
	Only total loss	Max	4	1.18 (0.72,1.93)	0.525	0.18 (0,2.12)	87 (0,99)
	Caries	12	2	1.87 (0.31,11.48)	0.497	0.99 (0,0)	48 (0,0)
	Caries	24	1	0.58 (0.17,1.94)	0.375	-	-
	Caries	36	2	1.72 (0.80,3.70)	0.165	0.15 (0,0)	45 (0,0)
	Caries	Max	4	1.49 (0.62,3.55)	0.372	0.56 (0,5.46)	74 (0,96)
	Caries progress under sealant	Max	1	HR: 0.7 (0.5,1.1)	0.10	-	-
	Sealant replaced by restoration	Max	1	HR: 0.7 (0.5,1.1)	0.09	-	-
	Sealant retreated	Max	1	HR: 0.8 (0.6,1.0)	0.07	-	-
	Outcome	**Mos**	**N**	**RR (95% CI)**	**P**	**tau^2 (95% CI)**	**I^2 (95% CI)**
Deciduous versus permanent dentition (referent)							
	Combined loss	6	3	2.93 (0.28,30.49)	0.368	3.036 (0,0)	72 (0,0)
	Combined loss	12	6	0.91 (0.23,3.54)	0.891	2.222 (1.166,11.080)	84 (73,96)
	Combined loss	Max	7	0.93 (0.31,2.83)	0.9	1.737 (0.909,7.380)	89 (82,97)
	Only total loss	6	1	1.16 (0.77,1.73)	0.478	-	-
	Only total loss	Max	1	1.16 (0.77,1.73)	0.478	-	-
	Outcome	**Mos**	**N**	**RR (95% CI)**	**P**	**tau^2 (95% CI)**	**I^2 (95% CI)**
Mandible versus maxilla (referent)							
	Combined loss	6	7	0.56 (0.27,1.16)	0.119	0.77 (0.40,2.97)	98 (97,100)
	Combined loss	12	14	0.93 (0.59,1.46)	0.741	0.57 (0.32,1.45)	99 (98,100)
	Combined loss	18	3	0.96 (0.68,1.36)	0.825	0.06 (0,1.85)	71 (0,99)
	Combined loss	24	7	0.88 (0.59,1.31)	0.529	0.20 (0,0.90)	96 (0,99)
	Combined loss	36	2	0.98 (0.76,1.25)	0.846	0.02 (0,10.59)	40 (0,100)
	Combined loss	Max	14	0.92 (0.62,1.37)	0.692	0.44 (0.25,1.11)	99 (99,100)
	Only total loss	6	4	1.03 (0.41,2.62)	0.946	0.54 (0,5.60)	72 (0,96)
	Only total loss	12	7	0.80 (0.50,1.27)	0.341	0.27 (0,1.00)	82 (0,95)
	Only total loss	18	1	0.89 (0.54,1.49)	0.664		
	Only total loss	24	5	0.93 (0.41,2.09)	0.857	0.56 (0,3.47)	93 (0,99)
	Only total loss	36	2	1.05 (0.60,1.85)	0.862	0.11 (0,0)	55 (0,0)
	Only total loss	Max	8	0.85 (0.54,1.35)	0.487	0.28 (0,0.92)	87 (0,96)
	Caries	12	4	0.66 (0.12,3.65)	0.633	1.91 (0,11.51)	66 (0,92)
	Caries	24	5	0.89 (0.33,2.43)	0.827	0.84 (0,4.22)	77 (0,95)
	Caries	36	2	2.30 (0.94,5.64)	0.068	0.25 (0,50.00)	56 (0,100)
	Caries	Max	8	1.28 (0.62,2.62)	0.503	0.74 (0,2.26)	80 (0,92)

	Caries under sealant	Max	1	HR: 0.7 (0.5,1.0)	0.07	-	-
	1st Re-seal need	Max	2	1.08 (0.44,2.62)	0.874	0.34 (0,0)	80 (0,0)
	2nd Re-seal need	Max	1	2.62 (0.24,28.64)	0.431	-	-
	Sealant replaced by restoration	Max	1	HR: 0.7 (0.5,1.0)	0.03	-	-
	Sealant retreated	Max	1	HR: 0.8 (0.6,1.0)	0.07	-	-
	Outcome	**Mos**	**N**	**RR (95% CI)**	**P**	**tau^2 (95% CI)**	**I^2 (95% CI)**
pPM1 versus pM1 (referent)							
	Combined loss	6	2	0.17 (0.05,0.58)	0.005	0.42 (0,44.48)	51 (0,99)
	Combined loss	12	2	0.12 (0.03,0.50)	0.004	0.71 (0,50.00)	62 (0,99)
	Combined loss	18	2	0.06 (0.01,0.33)	0.001	0.80 (0,50.00)	51 (0,99)
	Combined loss	24	2	0.16 (0.04,0.64)	0.01	0.68 (0,50.00)	64 (0,99)
	Combined loss	Max	2	0.16 (0.04,0.64)	0.01	0.68 (0,50.00)	64 (0,99)
	Outcome	**Mos**	**N**	**RR (95% CI)**	**P**	**tau^2 (95% CI)**	**I^2 (95% CI)**
pPM2 versus pM1 (referent)							
	Combined loss	6	2	0.53 (0.17,1.70)	0.287	0.44 (0,0)	58 (0,0)
	Combined loss	12	2	0.38 (0.14,1.07)	0.068	0.30 (0,50.00)	49 (0,99)
	Combined loss	18	2	0.33 (0.12,0.92)	0.034	0.29 (0,42.45)	48 (0,99)
	Combined loss	24	2	0.81 (0.26,2.55)	0.723	0.56 (0,50.00)	82 (0,100)
	Combined loss	Max	2	0.81 (0.26,2.55)	0.723	0.56 (0,50.00)	82 (0,100)
	Outcome	**Mos**	**N**	**RR (95% CI)**	**P**	**tau^2 (95% CI)**	**I^2 (95% CI)**
pPMs versus pM1 (referent)							
	Combined loss	6	4	0.44 (0.08,2.52)	0.356	2.24 (0,25.28)	84 (0,98)
	Combined loss	12	6	0.25 (0.12,0.52)	<0.001	0.55 (0,3.07)	83 (0,97)
	Combined loss	18	4	0.22 (0.05,0.89)	0.034	1.46 (0,14.06)	78 (0,97)
	Combined loss	24	6	0.34 (0.17,0.68)	0.002	0.54 (0,3.63)	89 (0,98)
	Combined loss	60	1	1.44 (1.09,1.90)	0.009	-	-
	Combined loss	120	1	1.19 (1.02,1.38)	0.031	-	-
	Combined loss	180	1	1.06 (0.97,1.15)	0.227	-	-
	Combined loss	Max	7	0.42 (0.21,0.83)	0.013	0.69 (0.32,3.51)	96 (91,99)
	Only total loss	6	1	3.96 (0.17,93.17)	0.393	-	-
	Only total loss	12	3	0.25 (0.03,2.41)	0.23	2.88 (0,50.00)	72 (0,98)
	Only total loss	18	1	1.33 (0.09,20.26)	0.836	-	-
	Only total loss	24	3	0.36 (0.06,2.11)	0.257	1.63 (0,40.50)	69 (0,98)
	Only total loss	60	1	1.60 (1.03,2.50)	0.037	-	-
	Only total loss	120	1	1.07 (0.81,1.40)	0.648	-	-
	Only total loss	180	1	1.08 (0.89,1.30)	0.438	-	-
	Only total loss	Max	4	0.52 (0.13,2.00)	0.341	1.37 (0,12.98)	81 (0,98)
	Caries	24	2	0.17 (0.03,0.86)	0.033	0.96 (0,0)	62 (0,0)
	Caries	60	1	0.02 (0.00,0.31)	0.005	-	-
	Caries	120	1	0.02 (0.00,0.14)	<0.001	-	-
	Caries	180	1	0.01 (0.00,0.10)	<0.001	-	-
	Caries	Max	3	0.07 (0.01,0.61)	0.015	2.79 (1.18,50.00)	82 (66,99)
	1st Re-seal need		2	0.30 (0.10,0.92)	0.035	0.51 (0,0)	77 (0,0)

	2nd Re-seal need		1	0.58 (0.05,6.34)	0.655	-	-
	Outcome	**Mos**	**N**	**RR (95% CI)**	**P**	**tau^2 (95% CI)**	**I^2 (95% CI)**
pM2 versus pM1 (referent)							
	Combined loss	6	2	0.93 (0.32,2.68)	0.892	0.40 (0,50.00)	68 (0,100)
	Combined loss	12	3	0.86 (0.29,2.53)	0.788	0.61 (0,17.09)	72 (0,99)
	Combined loss	18	2	1.03 (0.39,2.73)	0.947	0.37 (0,50.00)	74 (0,100)
	Combined loss	24	2	0.31 (0.02,5.99)	0.439	4.06 (1.05,1.05)	88 (66,66)
	Combined loss	60	1	0.40 (0.22,0.72)	0.003	-	-
	Combined loss	120	1	0.80 (0.63,1.02)	0.075	-	-
	Combined loss	180	1	0.69 (0.58,0.82)	<0.001	-	-
	Combined loss	Max	4	0.44 (0.11,1.80)	0.255	1.64 (0,19.74)	95 (0,100)
	Only total loss	12	1	0.60 (0.03,11.23)	0.732	-	-
	Only total loss	60	1	0.42 (0.17,1.06)	0.067	-	-
	Only total loss	120	1	0.78 (0.53,1.15)	0.213	-	-
	Only total loss	180	1	0.60 (0.43,0.84)	0.002	-	-
	Only total loss	Max	2	0.60 (0.22,1.61)	0.309	0.25 (0,0)	18 (0,0)
	Caries	24	2	0.91 (0.23,3.63)	0.898	0.86 (0.27,50.00)	87 (67,100)
	Caries	60	1	1.16 (0.65,2.05	0.618	-	-
	Caries	120	1	0.77 (0.48,1.23	0.267	-	-
	Caries	180	1	0.85 (0.60,1.22)	0.383	-	-
	Caries	Max	3	0.91 (0.40,2.06)	0.817	0.44 (0,14.69)	86 (0,100)
	1st Re-seal need	Max	2	0.33 (0.13,0.87)	0.024	0.24 (0,14.64)	81 (0,98)
	2nd Re-seal need	Max	1	0.97 (0.05,19.93)	0.986	-	-
	Outcome	**Mos**	**N**	**RR (95% CI)**	**P**	**tau^2 (95% CI)**	**I^2 (95% CI)**
dM2 versus pM1 (referent)							
	Combined loss	6	3	2.93 (0.28,30.49)	0.368	3.04 (0,0)	72 (0,0)
	Combined loss	12	6	0.91 (0.23,3.54)	0.891	2.22 (1.17,11.08)	84 (73,96)
	Combined loss	Max	7	0.91 (0.31,2.83	0.9	1.74 (0.91,7.38)	89 (82,97)
	Only total loss	6	1	1.16 (0.77,1.73)	0.478		
	Only total loss	Max	1	1.16 (0.77,1.73)	0.478		
	Outcome	**Mos**	**N**	**RR (95% CI)**	**P**	**tau^2 (95% CI)**	**I^2 (95% CI)**
dM2 versus dM1							
	Combined loss	Max	1	1.31 (0.83,2.06)	0.249	-	-
	Only total loss	Max	1	0.82 (0.47,1.45)	0.5	-	-
	Caries	Max	1	1.06 (0.45,2.49)	0.899	-	-

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Appendix 9. Subgroup analyses for meta-analyses including at least 5 studies.

					Outcome timing						**Sealant material**			
Comparison	**Outcome**	**N_{all}**		**SG**	**N_{SG}**	**RR (95% CI)**	**P**	**P_{SG}**		**SG**	**N_{SG}**	**RR (95% CI)**	**P**	**P_{SG}**
Deciduous versus permanent teeth (referent)														
	Combined loss	7		6 mos	1	1.10 (0.94,1.29)	0.250	0.153		CR	4	0.55 (0.10,3.00)	0.486	0.079
				12 mos	6	0.91 (0.23,3.54)	0.891			CR+F	2	2.19 (0.35,13.51)	0.400	
Maxillary versus mandibular teeth (referent)														
	Caries	8		12 mos	1	1.65 (0.68,4.02)	0.272	0.072		CR	4	0.91 (0.37,2.26)	0.834	0.004
				24 mos	5	0.89 (0.33,2.43)	0.827			CR+F	3	1.54 (0.41,5.82)	0.522	
				36 mos	2	2.30 (0.94,5.64)	0.503			GIC	1	2.68 (1.49,4.82)	0.001	
	Combined loss	14		12 mos	6	1.01 (0.40,2.53)	0.986	0.841		CR	7	1.17 (0.56,2.45)	0.684	0.458
				18 mos	1	0.98 (0.94,1.03)	0.426			CR+F	5	0.72 (0.42,1.21)	0.212	
				24 mos	5	0.87 (0.48,1.58)	0.642			GIC	2	0.99 (0.94,1.05)	0.796	
				36 mos	2	0.98 (0.76,1.25)	0.846							
pPMs versus pM1 (referent)														
	Combined loss	5		5						CR	4	0.33 (0.20,0.56)	<0.001	0.834
				0						CR+F	1	0.28 (0.08,0.91)	0.034	

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Appendix 10. Additional information to the systematic review.

Author contributions

SNP developed the study protocol, ran searches and extracted hits, did study selection, data extraction, risk of bias assessment, handled communications with trialists, did statistical analysis, assisted in the interpretation of results, wrote the first manuscript draft, approved the final version, and is the corresponding author, guarantor of the present review, and responsible for any updates. DD revised the study protocol, did study selection, data extraction, risk of bias assessment, revised the manuscript draft, and approved the final version. NK, KB, VW revised the study protocol, assessed in issues arising during study selection/data extraction/ risk of bias assessment, revised the manuscript draft, and approved the final version.

Post hoc changes from the registered protocol

-Data analysis: The relative risk was used over the initially set odds ratios for most of the binary outcomes, as it is more clinically relevant and easily understood. Two studies reported hazard ratios and were separately reported.

-Data analysis: Reporting biases (small-study effects, including publication bias) were planned to be assessed through the inspection of contour-enhanced funnel plot and with the Egger's weighted regression test [Egger et al., 1998], if at least 10 trials were identified. If hints of bias were identified sensitivity analyses were performed by including only bias free and/or the most precise studies. However, no such analyses could be performed, due to the limited number of included studies (no meta-analyses with least 10 studies).

-Data analysis: After the suggestion of an external reviewer during the paper's peer review, we also calculate the absolute risk reduction and relative risk reduction for the outcome of caries prevalence under sealed premolars and molars. This is done only for the statistically significant effect of premolars vs molars and is reported very shortly in the Discussion and declared as post hoc.

-GRADE assessment: following the skepticism of an external reviewer during the paper's peer review, we have decided to treat the included randomized trials as observational studies in the GRADE assessment, due to the observational nature of data extracted from included trials.